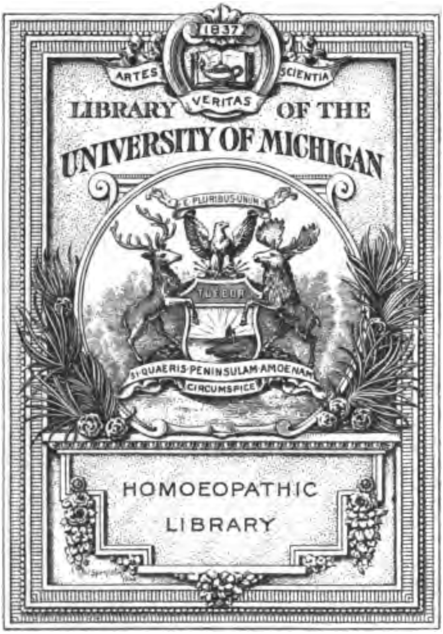
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A MANUAL

OF

PATHOLOGY

BY

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PREFACE

The purpose of this volume is not that it shall attempt to take the place of the more voluminous text-books on pathology, but that it shall enable the student especially to rapidly acquire the salient points of a subject. To this end the author has sought brevity, but has tried at the same time not to sacrifice clearness in the exposition of the material.

If the student finds that this manual fulfils the above conditions the author will have accomplished his purpose.

G. McC.

St. Louis, Mo., *August*, 1906.

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A MANUAL OF PATHOLOGY

PART I—GENERAL PATHOLOGY

CHAPTER I

PATHOLOGY

"**Pathology** is that subdivision of biology which has for its object the study of life in its abnormal relations." It is the science that treats of disease in all its aspects.

By disease is meant any condition in which there is a variation from the normal aspect of the organism; it may be either a structural or a functional deviation.

Pathology may also be divided into two large classes, one in which the changes are structural, a condition known as *morbid anatomy* and *histology*. The other is where the changes are functional, *morbid physiology*.

The main heading may be again subdivided into *general pathology*, that deals with abnormal processes common to the entire organism, such as inflammation, fever, etc., and *special pathology*, that includes the changes within special organs.

Under **etiology** are considered the conditions giving rise to disease. They may be either *predisposing* or *exciting*.

Predisposing causes are those that in any way lower the vitality of the individual and thus render him more susceptible; such as bad hygienic surroundings, poor food, bad air, noxious gases, fatigue, extremes of temperature, drugs, injury, pre-existing disease.

Exciting causes include mechanical forces, sudden extremes of heat and cold, electricity, poisons, parasites, and also certain mechanical abnormalities, such as defects in the heart-valves.

Although the causes are divided into these two classes, a predisposing cause if acting with great severity may readily excite disease.

The individual may be the seat of two diseases, one acting primarily and another following secondarily.

The latter may be either the direct result of the primary or may have nothing whatever to do with it. Infection of the lung by the tubercle bacillus gives rise to phthisis; later on there may be involvement of pleura or of intestine, or a person suffering from chronic nephritis will often die from a secondary pneumonia.

Traumatism may cause disturbances of function more or less marked according to the extent, severity, rapidity, and duration of its action.

If it takes the form of constant pressure, there will be malnutrition and atrophy of the part on account of the interference with the blood-supply. If the pressure is intermittent hyperemia may occur and hypertrophy take place.

When the force is sudden the lesions vary according to the instrument used. If sharp, there are lacerations; if dull, contusions.

According to the locality there may be fractures and concussion. In all these injuries there is greater or less destruction of tissue, followed by the phenomena of inflammation, with either recovery or death.

Temperature.—Following the local action of extreme *heat* a condition known as a *burn* results, in which there is relaxation of the blood-vessels, exudation of serum, and possibly of blood. The extent of the injury to the tissues depends on the degree of heat and its time of action. According to the extent, burns may be divided into four classes: (1) Hyperemia of the exposed surface; (2) extravasation of serum and liquefaction of certain cells, thus forming vesicles; (3) coagulation of the cellular protoplasm with resulting necrosis and

extension into the deeper tissues; (4) charring of the tissues and extensive, deep involvement.

Death may result from burns, either immediately from shock or later from exhaustion, from a perforating ulcer of the dudoenum, or from toxic substances formed either within the body or absorbed from the skin. There may be marked alterations within the blood and their action may prevent the kidneys from carrying on their functions.

The cause of the duodenal ulcer is not clear, but may depend upon thrombosis of some small vessel and subsequent digestion by the gastric juice. As a rule, a burn, even of the first degree, will prove fatal if it involves one-third the surface of the body.

If the exposure has been general the result will vary according to the cause, whether steam, dry air, or sun, etc. Exposure to dry air or sun may cause heatstroke or heat exhaustion. In the first there occur symptoms of heart failure, dyspnea, and coma, if severe. Usually the pulse is full and rapid, face flushed, very high temperature, dry skin, and labored breathing, unconsciousness and muscular relaxation. In heat exhaustion the skin is moist, cool, pale, pulse small and soft, unconsciousness unusual, and temperature may be subnormal.

Extreme cold will bring about conditions very similar to those resulting from heat, and will have various symptoms, according to whether the effects have been superficial or deep. In the former the tissue may completely recover, but in the latter the blood-vessels may be involved and gangrene follow.

The primary effect of cold is to bring about a contraction of the superficial blood-vessels. This, however, gives way to a paralytic dilatation, on account of which more blood enters the chilled part and the entire body will be affected.

If the tissue should freeze during the stage of contraction, the part would appear pale; if during that of dilatation, it would be swollen and dusky in color.

Electricity causes destruction of tissue either by the heat generated or by the resistance of the body to its passage.

Death may result instantly from disturbance of the ner-

vous system or there may be extensive and destructive burns. Sometimes there is involvement of internal organs.

X-rays when applied too closely or for too great a length of time occasionally give rise to a dermatitis or even to burns of the first, second, and third degrees.

Barometric pressure may cause disturbances if it be either greatly increased, as in deep-sea divers or caisson-workers, or diminished, as in mountain-climbers and in persons ascending in balloons. In the latter the blood shows an increase in the number of red corpuscles, in their specific gravity, and in their hemoglobic content.

Season also has a distinct effect upon disease; pneumonia and bronchitis being most common in winter, typhoid fever and malaria in spring, yellow fever and enteric disorders in the summer.

Intoxication.—A *poison* is a substance which when introduced into the living body in a relatively small amount will disturb the structure or functional activity. These substances may be formed within the body through faulty metabolism and give rise to *endogenous* or auto-intoxication; they may be introduced from without, *exogenous* intoxication. The endogenous may be (1) *immediate* and *indiscriminate* in their action or they may be (2) *remote* and *selective.*

1. The first group includes the *caustics* and *irritants*. Their effects are the more marked the greater the concentration, and may be purely local. The poison may, however, be absorbed and give rise to remote effects. In this class belong the salts of the heavy metals, a few vegetable substances, and some animal products.

The effects may vary from a slight reddening to marked necrosis and sloughing. They are brought about by abstracting the water from the tissue, by coagulating the albumins and forming definite compounds with the elements. The effect depends on various conditions both of the individual and of the poison. If a patient has been addicted to the use of a drug, a dose fatal to others may cause in him very slight disturbance. Sometimes a very large dose may cause vomiting, and the poison is in that way removed.

2. Many of the first group come secondarily into this class by being absorbed and taken up into the blood. They may unite with the hemoglobin or they may bring about *hemolysis*, a destruction of the red corpuscles.

When the poison combines with the hemoglobin, forming methemoglobin, the union is so close that the oxygen can no longer be taken up and supplied to the tissue. Death then results from a general asphyxia. Instead of death, cyanosis may develop, this commonly resulting from the use of coal-tar products.

Strychnin is selective in its action in that it stimulates the respiratory centers and the motor nerves. Bromids depress them.

Foreign bodies that are not living may cause disease by mechanically interfering with the functions of the body. The most important causes of disease are, however, *bacteria*, the lowest form of vegetable life. They are almost ubiquitous and give rise to many disturbances of function. It is not, however, always possible to prove the relationship between bacteria and disease. Koch has advanced four laws. They are: (1) The bacteria must be found in the diseased individual; (2) they must be capable of cultivation upon media outside the body; (3) pure cultures introduced into a healthy animal must produce the disease in the animal; (4) the bacteria must be recovered from the inoculated animal.

Diseases caused by bacteria are capable of transmission from person to person and are generally termed *infectious*. They may gain entrance into the body through abrasions of the skin and mucous membranes, through the air or by means of the digestive tract, through the genito-urinary tract, or they may be transferred from the maternal to the fetal blood in the uterus.

Animal parasites may frequently be the cause of disease. To this class belong the various intestinal worms, and certain blood organisms, as the plasmodium of malaria, the filaria, the trypanosomes, etc.

CHAPTER II

DEFECTS OF DEVELOPMENT

A malformation is any deviation from the normal embryonal development. This may be the result either of some disturbance taking place in the self-developing power of the embryo, or else due to some influence directly concerned with the maternal structures. The causes may be either internal, existing in the embryo itself, or external, those acting from without.

If the development is only slightly imperfect the condition is called a *malformation;* if marked, it is a *monster.* The defect may occur within an individual or there may be two or more united individuals, the latter being either double or triple monsters.

To have any serious malformation taking place, the causes must have begun to exert themselves very early in embryonal life. In such cases the lesions will generally be of such a nature that extra-uterine existence is impossible. It is probable that such take place before the third month.

The malformations brought about by external causes usually occur during the later period of fetal development. As a rule, they are not of sufficient gravity to prevent the child from living.

Some of the departures from normal occur in different cases, but with about the same appearances; these are spoken of as *typical* and are due generally to some internal cause, harelip being such an example. If the malformation is entirely unusual it is *atypical,* and results from external factors.

If the variation is one that is present in either parent it is spoken of as an inherited abnormality, as in the frequent

occurrence of extra fingers or teeth in successive generations; is also seen in the way in which certain diseases are transmitted from parent to offspring.

If the abnormality passes over one or two generations before reappearing, the condition is known as *atavism*.

Varieties of Congenital Malformation.—The chief single forms of deviation are divided as follows:

1. *Aplasia*, or complete failure of development, which may be either general or local. If general, *abortion* usually results and the embryo is cast off. It may, however, be infiltrated with lime salts, forming a *lithopedion*. Examples of the local form are absence of parts of the body, as fingers, toes, and internal organs. This condition may prevent life, as in the absence of the brain or heart.

2. *Hypoplasia* is the failure of parts of the body to reach their full development, as in small size of limbs or of the brain. It is seen in cases where one kidney may be very large and the other very small.

3. Incomplete union along the line of closure of the fetal arches may be anterior, posterior, or lateral, such as extrusion of viscera, spina bifida, and harelip.

4. There may be an abnormal union of parts, as of the lower extremities.

5. Occasionally there is a duplication of parts, particularly of the digits; sometimes of the internal organs, as the spleen and pancreas.

6. Abnormal location of viscera. In these cases all the single organs are transposed, the heart and spleen on the right, the liver on the left side.

7. Obstruction of the external openings, mouth, anus, vagina, etc.

8. Persistent misplaced fetal structure, which may eventually give rise to neoplastic formations, usually cystic.

9. Anomalies of sex—hermaphroditism, which may be either true or false. In the early stages the embryo is bisexual, but finally one set of organs undergoes a perfect development, with slight traces only of the subsidiary organs. In the true form both sets of organs would be present, well devel-

oped. This condition is so rare that it is said not to exist, one case only having been reported.

In false hermaphroditism the malformation depends upon abnormalities of the external genitalia.

Double Monsters.—In these there is a duplication of the whole body, the halves being attached to each other, or a duplication of either caudal or cephalic end. Such monsters are always of the same sex and are usually joined at corresponding parts, as head, thorax, or sacrum. They arise from a single ovum and blastodermic vesicle, and the cause that determines their formation must exert its influence at the earliest stage of development, probably during the formation of the primitive streak and medullary groove.

They may result from:

1. Two embryonic areas arising within a single blastodermic vesicle and continuing to grow.

2. Two primitive streaks and two medullary folds arising within a single embryonic area and either remaining separate or merging.

3. A single primitive streak with either partial or complete doubling of the medullary groove.

4. The duplication may take place late in the development and affect only single parts.

The first three cause abnormalities along the main axis of the body; in the fourth, the variations lie to one side.

Twins and triplets in a way belong to the class of monstrosities, as they are a reversion to the lower types, in which multiple births are common.

The twins may be equally developed and of the same size, or one may be larger and more advanced. They will in the first case usually live; in the second they sometimes continue to exist.

The varieties of double monsters are named by adding the word "pagus" (from *pag*, meaning "to fasten") to the name of the part of the body by which they are attached, as xiphopagi, when joined by the xiphoid cartilage; cephalo-pagus if by the heads.

These monstrosities may or may not live, according to

the development of the internal organs. In many cases each individual has had well-developed and separate organs and the two have lived for many years.

Sometimes one of the twins may take up the nutrition at the expense of the other, with subsequent increase in size. The larger of the two is called an *autosite*, and the other a *parasite*. The latter is generally imperfectly developed.

The abnormalities of the various important organs will be considered in their respective chapters in Part II.

CHAPTER III

DISORDERS OF METABOLISM

By *metabolism* is meant those physiologic processes brought about in living tissue by means of which the individual is able to form new tissue and reintegrate the old. Under this head comes the rejection of those substances that are unfit for use in the bodily economy.

When the tissues are unable to carry on these molecular exchanges a pathologic condition exists. This may be either functional or structural, the latter generally being secondary to the former.

Metabolism may be divided into two classes according to whether simple substances are built up into complex, or the complex broken down into the simple. The building up or constructive variety is called *anabolic metabolism;* the breaking down or destructive, *catabolic metabolism.*

By means of catabolism the "end products," those substances not required by the body, are formed; such as urea, water, etc. Anabolism is concerned in the rearranging of molecules so as to render them suitable for food.

A food is a substance that will form new or reintegrate old tissues. It may be either in excess or in diminution, or may vary in quality, the amount required depending upon the activity of the individual.

The assimilation of food depends upon the presence within the gastro-intestinal tract of certain digestive ferments, which may vary greatly in quantity.

The *proteid* substances are acted upon by the pepsin in the stomach and the trypsin from the pancreas. Pepsin acts in an acid medium, trypsin in an alkaline. The necessary acid in the stomach is the hydrochloric. Changes from the nor-

mal amount of pepsin are unusual, but there may be great variations as far as the acid is concerned. It may be increased, *hyperchlorhydria;* diminished, *hypochlorhydria;* or absent, *achlorhydria.* If absent or much diminished, the food not being properly digested will undergo fermentation. If there be any obstruction at the pylorus the stomach will tend to dilate.

The *carbohydrates* are acted upon first in the mouth by the salivary ferment, *ptyalin;* then in the intestine by *amylopsin,* a ferment derived from the pancreas.

The *fats* are acted upon by *steapsin,* a pancreatic ferment, and by the bile.

The condition of the individual depends upon the assimilation of the food, which may be abnormal in quantity or quality.

If the quantity taken up by the individual is diminished either by lack in amount or by being deflected from its proper channels, certain pathologic conditions will result. These may be starvation, in which case the bodily weight diminishes, the temperature falls, and the energies all fail. At first the reserved food is called upon. The circulating proteids are first used up, then the glycogen, and afterward the fats and the muscles. The heart and the central nervous system are the last structures to be involved. The organs become smaller, the excretions and secretions are gradually suspended. In the blood the leukocytes become much fewer, although the red cells appear in normal number. This is probably due to the loss of the blood-serum. Death takes place slowly, either from exhaustion, disorders of metabolism, or by terminal infections.

In *marasmus,* a term applied to babies and old people, the wasting away takes place more slowly than in starvation. In it the trouble is very frequently not due to lack in quantity of food but to improper assimilation.

If during the course of a definite disease these symptoms of slow starvation appear, the condition is called *cachexia.* In it there is a peculiar yellowish color of the skin and also a marked anemia.

Rachitis or *rickets* is a condition of childhood that is indicated by structural changes of the bones, particularly those of the pelvis and of the lower extremities. There is a lack of proteids and of inorganic salts. It is generally accompanied by gastro-intestinal disturbances.

If larger amounts of food are taken than are necessary for the bodily requirements, the excess will be carried through the intestines unacted upon. It will cause an overfilling of the blood-vessels or else there will be an excessive deposit of fatty tissue, this condition being known as *obesity* or *polysarcia*. It may be either the result of excessive assimilation of the carbohydrates or of diminished oxidation of the fat-forming substances.

In *asphyxia* there is a lack in the amount of oxygen and an increase in the carbon dioxid. In this process there is first a period of increase in the inspiratory efforts, then in the expiratory, and finally exhaustion. After death the heart, particularly the right side, is found to be distended with blood.

Dyspnea is a slight lack of oxygen, sufficient to stimulate but not to depress the respiratory centers. *Cyanosis*, a bluish color of the skin, particularly of the face, then appearing. *Apnea* is a condition in which there is a period when no respiratory action takes place.

Abnormalities in the secretions of the organs may cause marked disturbance. The secretions may be either *internal* or *external*. The external pass directly from the glands by means of ducts. The internal pass slowly into the blood, which carries them to all parts of the body.

The *thyroid secretion*, when lessened or absent, gives rise to the condition known as *myxedema*. In this the skin becomes much swollen and firm, particularly in the region of the face. The skin will not pit on pressure nor are the dependent portions affected. The hair frequently falls out, the voice undergoes changes, and there are commonly decided disturbances of mentality. If sheep's thyroid gland is given in such cases, there is frequently a decided improvement.

Cretinism is a very similar but more severe condition resulting from disease of the thyroid during intra-uterine life or in early childhood, usually appearing during the first year. The child does not develop, remains a dwarf, there is more or less complete loss of mind, the lips are very thick, tongue large, and the abdomen very pendulous. Frequently several members of a family are found to be suffering from it. The state is also occasionally markedly hereditary.

If the thyroid secretion be increased, there may result *exophthalmic goitre*, or Basedow's disease. It is characterized by enlargement of the thyroid gland, paroxysms of palpitation of the heart, bulging of the eyes, and nervous excitement. In this the administration of sheep's thyroid increases the symptoms.

The relationship between the thyroid gland and general disease is not clearly understood. There appears to be distinct bearing upon the nervous system and also upon the metabolic processes taking place within the body. The active principle seems to be "thyroidin," a substance that contains nearly 10 per cent. of iodin.

The secretion of the *adrenals* seems of marked importance, as disease of or removal of those bodies causes severe disturbances in the individual. If completely removed, collapse and death occur within a few hours. When the breaking down has taken place slowly, a condition known as *Addison's disease* results. In it there is an increasing weakness, accompanied by anemia, emaciation, and a peculiar bronzing of the skin and mucous membrane of the mouth.

The action of the adrenal secretion seems to be more upon the vasomotor condition. When applied locally the vessels will contract, and if injected into the circulation will cause a rise in blood-pressure. This is due to the contraction of the arterioles.

Whether or not it has a relation to the pigmentation of the skin and to the cachexia is not settled.

The secretion of the *pituitary body* seems to bear definitely upon the nutrition of the tissues. When diseased the condition of *acromegaly* is generally present. In it there is a

marked enlargement of the bones of the face and of the extremities. The enlargement is due to an actual hypertrophy of the parts involved. Accompanying this there is usually some interference with speech, and the memory is slightly affected.

In the *pancreas*, besides the three external secretions, there is also an internal one. It seems to be chiefly concerned in carbohydrate metabolism; it is a glycolytic ferment.

Diabetes is a disease in which the carbohydrates are not properly assimilated and it is characterized by the persistent appearance of sugar in the urine. In this way it differs from alimentary glycosuria, in which the sugar appears transitorily. This is due to an incomplete arrest of sugar in the liver, some of which escapes into the urine.

In diabetes there is always a preceding increase of sugar in the blood, *glycemia*. About 0.1 per cent. is normal; in increased amount it acts as a poison upon the protoplasm of the cells and increases nitrogenous metabolism. The excess is eliminated by the kidneys and appears in the urine as dextrose, no matter in what form the sugar was consumed.

The generally accepted opinion as to the cause of diabetes is that it is due to disease of the pancreas. Extirpation of that organ gives rise to a glycosuria closely resembling diabetes and terminating fatally.

The structures most intimately concerned are the islands of Langerhans. These are most numerous in the tail or splenic end of the gland and are supposed to regulate the metabolism of sugar. If the lesion involve these structures, then diabetes ensues; if, however, the head end is affected there may be no glycosuria, as the islands are not found in that portion.

The lesion of the islands belongs to the group of hyaline degenerations. There is the formation of a homogeneous substance that stains with the acid dyes but does not give the amyloid reaction.

There may also be an interstitial change that affects the parenchyma of the organ as well as the islands of Langerhans.

All cases of diabetes cannot, however, be ascribed to disease of the pancreas, as injuries to the floor of the fourth ventricle of the brain will give rise to the same symptoms.

Disorders of excretion may give rise to abnormal conditions, either by valuable products being thrown off unused or by the retention of harmful substances.

In the daily excretion of urine from 30 to 40 grams of urea are disposed of. If this substance is retained within the body, *uremia* results. More recent investigations would indicate that it is not so much the retention of urea that causes the symptoms as the presence of the compounds from which urea is formed, particularly ammonium carbamate.

In the urine there are several toxic substances. Although no one of these alone will produce uremia yet the combination of all may cause it.

Uremia may be acute or chronic. In the former there develop severe convulsions, vomiting, blindness, and coma, with death frequently. In the chronic form there is headache, drowsiness, and slowly developing coma.

A condition closely allied is that of eclampsia, in which pregnant women present symptoms similar to those of uremia. It may be due to the retention within the blood-serum of toxic substances probably derived from the placenta.

Gout or *podagra* is a disease in which there is deposited within the joints, in the articular cartilages, uric acid and its compounds. It generally affects the small joints of the hands and feet, particularly the big toes. These salts may be deposited elsewhere, as tophi in the cartilages of the ear, and in the meninges. As a result of these deposits the joints may be much deformed. Lesions of other portions of the body are usually present. There is a marked tendency toward the formation of connective tissue in the form of interstitial nephritis and of arteriosclerosis; fatty changes also take place in the heart and liver. Gout usually appears after middle life in those who have lived very well, drunk plenty of wine, and have not taken exercise. It is a chronic disease, but exhibits periods of acute and painful inflammation lasting several days.

The salts concerned are the sodium biurates and quadriurates, uric acid existing in the blood in the form of the latter. The soluble quadriurates circulating in the blood, if in the presence of uric acid and sodium salts in excess, are precipitated as insoluble crystalline biurates.

In *oxaluria* and *phosphaturia* there is an excess of either oxalic acid salts or of phosphates. The presence of oxalic acid is thought by some to be due to the amount present in the vegetable matter consumed, while others think it is the result of deficient oxidation of the carbohydrates. It is of chief importance in the formation of calculi, it being precipitated in the crystalline form mainly when there is an increased amount of calcium in the urine.

The phosphoric acid exists in the form of the phosphates of magnesium, ammonium, and sodium. These may form calculi in the bladder when they occur in excessive amount in an alkaline urine, as they remain in solution if the reaction is acid.

Acetone and *diacetic* acid are often found in the blood and urine in the later stages of diabetes.

The *bile* may vary in amount and consistency and may be prevented from passing into the bowel. The normal amount secreted varies from 500 to 1000 c.c. in a day. It is composed chiefly of water, but contains bile salts, cholesterin, lecithin, fat, and coloring substances. The salts are the glycocholate and the taurocholate of sodium. The important pigments are bilirubin and biliverdin, both of which are derived from the blood. Bilirubin undergoes oxidation to form various other pigments. It resembles hematoidin, and the toxic effects of the retention of bile seem to depend upon its presence, as when the bile is freed from its coloring-matters by filtration it is only one-third as toxic as in its original condition.

If there should be any obstruction to the outflow of bile the condition known as *icterus* or *jaundice* follows. This obstruction may result from a catarrhal condition or a stenosis of the bile capillaries, inflammations of the common bile-duct, or of the papilla. It may be due to foreign substances, such as gall-stones, inspissated mucus, round-worms, or

tumors within the large duct, or to pressure upon it from without. The jaundice is due to the absorption of the bile into the general circulation by means of the veins or lymphatics. A large amount of it is eliminated by the kidneys, while the excess is deposited within the connective tissues.

As a result of the absorption of the bile the skin is at first yellow, but if the condition continues for some time the pigment oxidizes and becomes greenish in color. This discoloration will be seen in the sclera, the lining of the arterial system, the mucous membranes, and in most secretions and exudations, normal or pathologic. The heart's action is frequently slowed (bradycardia) to 50 or even 20 beats a minute.

The effect upon digestion may be quite marked. There is found an excessive amount of fat in the feces. The stools become very light in color, due to the absence of hydrobilirubin, and may be very offensive. There may be some interference with the outflow of the pancreatic enzyme, which would have a distinct effect upon the amount of fat present and also upon the color of the feces.

Sometimes there are marked nervous symptoms, probably the result of the presence of the biliary acids and salts in the circulation rather than due to the pigments.

Another form of jaundice is that of hematogenous origin. It occurs when no obstruction to the outflow of bile can be found. Although bile cannot be formed in any other place than in the liver cells, there are cases in which a general yellowish discoloration takes place without any hepatic lesion being present. It occurs in certain infectious diseases, as in yellow fever, malaria, etc., in poisoning by venom and toluylendiamin, and in the new-born in the form of icterus neonatorum. In all these conditions, particularly in the last named, there is a very marked destruction of the erythrocytes. The blood-pigment is changed into bile-pigment and thus stains the tissue. This form may be due to some nervous disturbances that cause a contraction of the circular muscles of the bile-ducts. It may be that there is an increase in the viscosity of the bile on account of the presence of the blood-pigments, and in that way the ready outflow is

prevented. It has also been shown that the concentration of the bile is associated with an inflammatory condition of the bile-ducts.

Besides the secretion of bile the liver also forms urea and glycogen, but these two latter bodies are carried off in the blood.

Disturbances within the intestine may bring about a condition of putrefaction accompanied by various symptoms of self-intoxication. The feces are made up of the remnants of digestion and of waste products. Their odor is due to the presence of indol and skatol.

The intestinal disturbances are due chiefly to the presence of bacteria and their products. Fermentation may take place in the stomach with the formation of acetic, lactic, or butyric acids, or of alcohol. It results from the breaking down of the carbohydrates. In the intestine the proteids may undergo putrefaction and produce amido acids, or aromatic bodies, as acetone, tyrosin, cresol, skatol, and indol. Ptomains may be formed and give rise to many symptoms. These bodies resemble quite closely many of the vegetable alkaloids and give rise to symptoms similar to those resulting from the drugs.

As a result of these disturbances *diarrhea* may occur. In this condition the feces are too soft and the bowel movements too numerous. It is an attempt to free the body of the irritating substances and may relieve the patient. The diarrhea may be due to increased rapidity of peristalsis, increased secretion of the intestine, diminished absorption by the large intestine, or disturbances of the controlling nervous mechanism, these depending upon many causes. These may be mechanical, inflammatory, infectious, obstructive, hepatic, and pancreatic.

Constipation or *coprostasis* is a condition in which the bowel movements are infrequent and the feces hard and dry. If the retained waste products are absorbed into the body, *copremia*, a form of auto-intoxication, results. Constipation may be due to obstruction, to impairment of peristalsis, abnormal consistency of the feces, or to impaired sensibility of the center of defecation in the spinal cord.

CHAPTER IV

CIRCULATORY DISORDERS

The circulation of the blood is maintained chiefly by two forces—the rhythmic contraction of the heart muscle, and the elasticity of the arteries. Other factors concerned are the compression of the veins by the muscles and the inspiratory action of the chest.

As these are the chief factors, any abnormality within them will bring about more or less general disturbances of the circulation. To these may be added alteration in the quantity or quality of the blood itself. According as to whether the effect is more marked in the systemic or in the pulmonary circulations the disturbances are more or less widely distributed.

The circulatory disorders may be *cardiac* in origin and either the result of *muscular* or *valvular* lesions. If muscular, there may be an *excessive* or, what is more common, a *diminished* action.

The former is seldom lasting, but while present causes a rise of blood-pressure, an increased amount of blood within the vessels in the part involved, and an increase in the rate of flow. If the overaction should be long continued, as a result of hard work or by constant stimulation, there would be hypertrophy of the left ventricle.

Diminished activity is more common and more important than the above. It may be brought about in many ways. It may be the sequel of a heart muscle weakened by the infectious fevers or other diseases, by poisons, by lack of nourishment caused by anemia, or by a blocking of the coronary arteries. It may be the result of nervous disturbances with no apparent lesion of the muscle, or it may be the result of some valvular disorder.

The valvular lesions and their sequelæ will be discussed in another chapter.

Sometimes it results from pressure from the outside—that exerted by collections of fluid in the pericardium, in the pleuræ, or by tumors or adhesions.

As a result of the weakened circulation there is an accumulation of blood in the venous circulation. If the failure is of the left ventricle, there will be a damming back of the blood in the left auricle and in the pulmonary circulation. If the right heart remains capable, the engorgement will go no further, but when it fails the right auricle becomes distended and a condition of general passive congestion ensues.

In all cases there is a decrease of arterial and an increase of venous pressure.

When the heart's action has become much weakened it will be found that the blood tends to gravitate to the more dependent portions, giving rise to *hypostatic congestion.* It occurs in the late stages of severe fevers and when death has taken place very slowly. The dependent tissues will become livid through the accumulation of blood, edematous from the escape of fluid from the blood-vessels, and sometimes bedsores may result. A frequent occurrence is a collection of blood within the lungs, a condition known as hypostatic pneumonia.

The changes within the *arteries* may be either *organic* or *nervous* (vasomotor). Their elasticity may be diminished, and their caliber increased or diminished. The alteration in caliber may be due to changes within the tissues or to disturbances of the vasomotor control.

If there is a paralysis of the controlling nerves, the vessels dilate and hyperemia results. On the other hand, stimulation will cause contraction and subsequent anemia. When sufficiently marked, there will be an increase in the blood-pressure, interference with the heart's action, and venous congestion.

The most common *organic* disturbance is a sclerosis of the vessel wall, a condition leading to constant interference with the arterial circulation. Generally a hypertrophy of

the left heart follows. If, however, the sclerotic changes are very widely distributed, instead of hypertrophy there may be a dilatation, on account of the resistance being too great for the heart to overcome.

Changes in the *quantity* of the blood, either an increase or a decrease, are generally only temporary, and soon readjust themselves, either through a contraction or a dilatation of the vessels.

Alterations in the *quality* have a marked effect upon the circulation, probably through the direct action of the toxic substances upon the vessel walls or upon the terminal nerve filaments.

Hyperemia.—*General Hyperemia.*—There may be an increase throughout the body of the total volume of blood. This seldom remains for any length of time, as the various excretory structures of the body get rid of it. The condition known as plethora is the result of persistent overeating and drinking. Is usually associated with a hypertrophy of the left ventricle.

Local hyperemia is an increase in the amount of blood in a part of the body. It may depend upon either an increased supply to the part or be due to a diminished outflow—in one case a dilatation of the arteries, in the other an obstruction of the veins. The first is known as *active* or *arterial*, the second as *passive* or *venous* hyperemia.

Active hyperemia is an excess of arterial blood in a part. It occurs with increased functional activity and increased metabolism. It may be brought about through the central nervous system or by direct stimulation of the peripheral nerves. Any pathologic condition that will bring about a local dilatation of the arteries will cause active hyperemia.

The spinal cord or a nerve may be pressed upon as the result of a tumor or of an injury, and a paralytic dilatation occurs. The same condition follows the use of certain drugs acting peripherally either upon the muscular coat of the artery or upon the local nervous mechanism, or both.

In active hyperemia the part affected is redder than normal and more or less swollen as the result of the increased

amount of arterial blood that it contains. The temperature is higher than in the surrounding parts, but never higher than that of the internal organs. There is also an increase in the rate of the blood-flow.

This form of hyperemia if continued for some time is followed by (1) hypertrophy of the part on account of the increased nutrition, (2) parenchymatous degeneration from

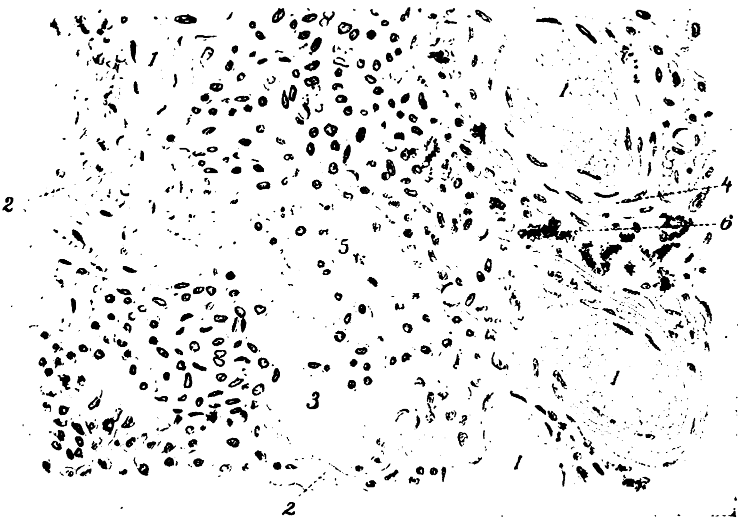


FIG. 1.—PASSIVE HYPEREMIA OF THE LUNG. × 250 (Dürck).

1, Ectatic and distended blood-vessels, filled with blood; 2, engorged and tortuous capillaries; 3, lumen of alveolus; 4, increased interlobular connective tissue; 5, cells, containing blood-pigment, within the alveolar lumen; 6, free, amorphous blood-pigment.

over-nutrition or over-stimulation of the cells, and (3) a proliferation of the connective tissue around the blood-vessels.

It is found as one of the phenomena of inflammation. Postmortem, it cannot be recognized on account of the contraction of the arterial walls, which drives out the blood. It may persist in the kidneys.

Passive hyperemia is an excess of venous blood in a part. It is the result of a distention of a vein on account of some obstruction to the outflow of the blood. This can be caused by obstruction within the veins or capillaries, as by thickening of their walls, by thrombi, or by pressure from without, as from a tumor. A common cause for general passive hyperemia is a lesion of the heart-valves. The circulation will continue slowly unless the venous pressure becomes as great as the arterial, when it will stop, a condition known as *stasis*.

A part the seat of passive hyperemia becomes cyanotic, swollen, edematous, cooler than normal, and its function less. The rate of blood-flow is lessened. The edema is due to the escape of fluid from the blood. If severe, red corpuscles may escape.

Following long-continued passive hyperemia the tissues will undergo a fatty degeneration, on account of the decreased nutrition, or even necrosis and gangrene may result. There may also be some increase in the amount of connective tissue. Pigmentation from escaped hemoglobin is not uncommon—*brown atrophy*.

When *stasis* occurs the blood-corpuscles slowly collect in the smaller vessels, the plasma is exuded, and the cells become packed closely together. Finally the outline of the cells cannot be seen and the vessels appear to be filled with coagulated blood. Such is not the case, as when the circulation is re-established the corpuscles separate and move along as usual.

Local anemia or *ischemia* is the condition in which the part contains less than its normal amount of blood. It is most commonly due to obstruction by pressure of the flow of blood into a part. This may be due to tight bandaging, pressure from a tumor, or to thrombi or emboli, or to changes in the wall of the vessel.

Disturbances of the vasomotor system may bring about marked lesions. If there is a good collateral circulation the area to which the obstructed vessel goes may show very slight change. If such is not the case, infarction may fol-

low. An anemic area is pale in color, temperature lower, and functional activity decreased.

Hemorrhage is the escape of all the constituents of the blood through the walls of the heart or of the blood-vessels. It is divided into three classes, according to the vessel from which it escapes, as *arterial*, *venous*, or *capillary*.

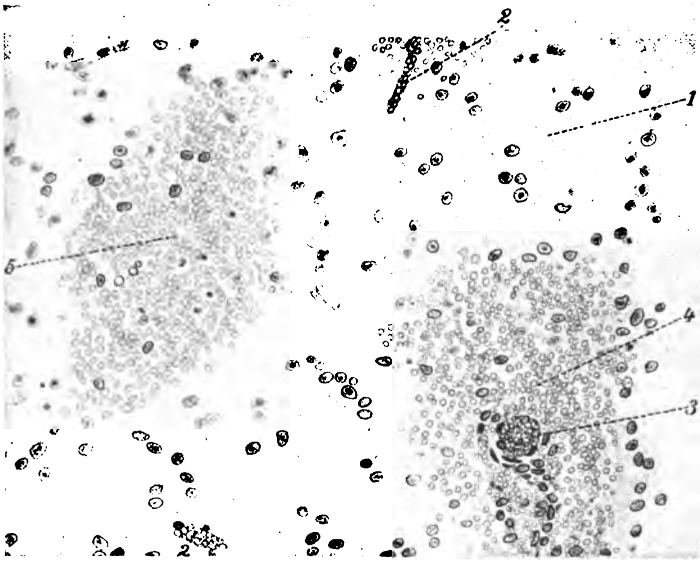


FIG. 2.—MULTIPLE CAPILLARY HEMORRHAGES IN THE CEREBRUM. Hemat.-eosin. × 270 (Dürck).

1, Cerebral substance; 2, engorged capillaries; 3, small artery with hemorrhagic infiltration of its walls; 4, hemorrhage by diapedesis in the tissues around a small artery; 5, smaller hemorrhagic foci without any connection with any blood-vessel visible in the section.

It may occur by *rhexis*, in which case there is a demonstrable destruction of the vessel wall, or by *diapedesis*, when there is no discoverable lesion. The latter form occurs only from veins and capillaries. The method of escape of the corpuscles is not clear, but is generally supposed to take

place through the stigmata of the lining endothelium. Hemorrhage by rhexis may be *primary* or immediate, and *secondary* or recurrent; the first following immediately, upon laceration of the vessel wall, the second occurring some time after the original injury.

Hemorrhages may also be designated by special terms according to the area involved. *Petechiæ* are minute, circumscribed hemorrhages. *Ecchymoses* are of moderate extent; are what are commonly known as bruises. *Extravasations*, *suffusions*, and *sugillations* are conditions in which extensive areas are implicated. A *hematoma* is a collection of blood within a solid tissue. A *hemorrhagic infarct* is a circumscribed hemorrhage within tissues, the result of the obstruction of an end-artery.

A hemorrhage may also have a special name according to its locality. According to the cavity in which it collects there may be a *hemothorax*, *hemopericardium*, etc. According to its method of escape from the body it may be known as *epistaxis*, bleeding from the nose; *hemoptysis*, from the lungs; *hematuria*, from the urinary tract, etc.

A peculiar form of hemorrhage is that known as *hemophilia*. In it no lesions can be discovered, but severe bleeding takes place as the result of most trivial injuries. It is generally hereditary, and transmitted through the daughters to their male descendants. The reason for the bleeding may be that the coagulability of the blood is decreased, but there may also be changes both in the blood and the vessels.

Hemorrhage by rhexis may be caused by: (1) *Increased blood-pressure*, particularly in those cases in which, the blood-vessel walls being diseased, their elasticity is diminished. (2) *Disease of the vessels*, in which the walls become so weak that they are unable to withstand the normal pressure. (3) *Traumatism*, injury of some form sufficient to cause a lesion of the vessel wall.

Hemorrhage by diapedesis may follow in the course of (1) certain *diathetic* diseases, as scurvy, purpura hemorrhagica, leukemia, hemophilia, etc.; (2) in severe *inflam-*

mations; (3) in severe *hyperemia,* either active or passive; (4) in certain forms of *poisoning,* particularly that by snake-bite; (5) *alterations of innervation;* (6) in *hemophilia.*

Spontaneous arrest of hemorrhage takes place in two ways: (1) When a vessel is injured its walls contract, and the lumen is diminished in size. The vessel also being elastic retracts within the surrounding tissues. (2) The blood coming in contact with abnormal surroundings coagulates, just outside, then upon, and finally within the vessel; this latter being known as a *thrombus.* In this way the vessel becomes plugged and the bleeding ceases. Another factor is that, as a result of the escape of large amounts of blood, the heart becomes weaker, even to a point where syncope may result; following this the blood-pressure falls and is unable to displace the clot.

The *results* of hemorrhage vary according to the amount of blood lost. If the amount has been small, there will be no ill effects; if comparatively large, weakness and unconsciousness; if very large, death will result from cerebral anemia. When the blood collects within the tissue, various changes take place. It undergoes coagulation, a condition in which fibrin factors acted upon by fibrin ferments form a solid body known as fibrin. The greater the amount of fibrin, the more difficult is it for the tissue to recover. The fluid elements are first taken up, by absorption, by the lymphatics. The corpuscular elements and the fibrin break up, hemoglobin is set free, and the particles are scattered through the tissue. The greater part will be slowly removed by the phagocytes, but some will remain. If the coagulation has been extensive the tissues may undergo a liquefaction necrosis, giving rise to a cyst.

Thrombosis is the coagulation of the blood within the vessels during life. It may depend upon changes within the blood, changes in the cardiovascular structures, and diminution of the velocity of the blood-flow.

The changes of the blood are those which tend to increase its coagulability. Certain chemical and physical substances when in the circulation may liberate fibrin ferments and

thus cause thrombosis. The toxins of pneumonia and of diphtheria are especially active.

The lesions of the vessel walls are particularly important. Fibrin will be deposited upon the wall of the heart or blood-vessels whenever the nutrition of the endothelium of that wall is impaired. Diseases leading to the roughening of the endothelium, particularly arteriosclerosis, are important causes. Inflammation of neighboring structures may bring about changes within the intima. Ligation of a vessel causes an injury to the internal coat and in that way predisposes to coagulation.

Diminution of the blood-flow may result not only from cardiac disturbances but also from conditions causing a decrease in the lumen of the vessel. As the current slows the leukocytes tend to adhere to the wall of the vessel, blood-plates make their appearance, and fibrin is deposited. The nutrition of the endothelium suffers, changes take place in the wall, and another factor in thrombosis then arises. The appearance of a thrombus depends upon the number of red corpuscles contained within it, and that rests upon the varying rapidity of the blood-current at the time of formation. It is generally made up of superimposed layers of fibrin.

If the blood were passing through the vessel with *considerable velocity*, the thrombus would be grayish-white in color, and on section would show well-marked lamination. This is called a *white thrombus*.

If the blood were moving less rapidly, varying numbers of red cells would be entangled in the fibrin and the color would be brown or grayish-red, giving rise to a *mixed* thrombus.

If it is formed in a short time from blood that is *barely moving*, a *red* thrombus will result.

A true thrombus differs from a post-mortem clot in that the latter is moister, is never adherent to the vessel wall, and never laminated. It may show a division into a pale and dark portion as a result of the coagulation taking place after the heavier red corpuscles have sunk.

Thrombi may be classified according to their *etiology* as:

1. *Infectious*—those depending upon the entrance of bacteria into the circulation.
2. *Mechanical*—foreign bodies free from organisms.

According to their period of *formation* as:

1. *Primary* or *initial* thrombi.
2. *Secondary* or *consequential*, depending upon a pre-existing thrombus and usually extending to the first collateral branch of the blood-vessel.

According to their *morphology* as:

1. *Central*, *occluding*, or *obstructing*—formed by the coagulation of the entire mass of blood contained within a certain portion of the vessel.
2. *Parietal*—when attached to the wall of the vessel but not completely obstructing it.
3. *Valvular*—parietal thrombi that have become partially detached.
4. *Channeled* or *tunneled*—ones in which there still exists a lumen through which the blood can pass. May be the result of secondary changes in old thrombi.
5. *Ball*—thrombi that lie free within the cavities of the heart, usually in the auricles.
6. *Polypoid*—ball thrombi with pedicles.

Metamorphoses of Thrombi.—The ultimate fate of thrombi depends upon whether they are septic or aseptic. If septic, they must undergo disintegration. If aseptic, they may undergo *organization*—a condition that is not a transformation into, but is a replacement by, connective tissue.

They may undergo a central *liquefaction* or *softening*. The interior is broken down, blood-pigment set free, and leukocytes in varying numbers are present.

Calcification, particularly of small thrombi, giving rise to either *arterioliths* or *phleboliths*, according to whether they occur in arteries or in veins.

The connective tissue that replaces the thrombi will gradually undergo contraction until only a hard fibrous mass remains; the original lesion becoming converted into a scar.

The new tissue is derived from the endothelium of the

blood-vessel. As it forms, the thrombus undergoes absorption and breaks down into a mass, the granules of which are removed by the leukocytes.

If the thrombi contain living organisms they will be car-

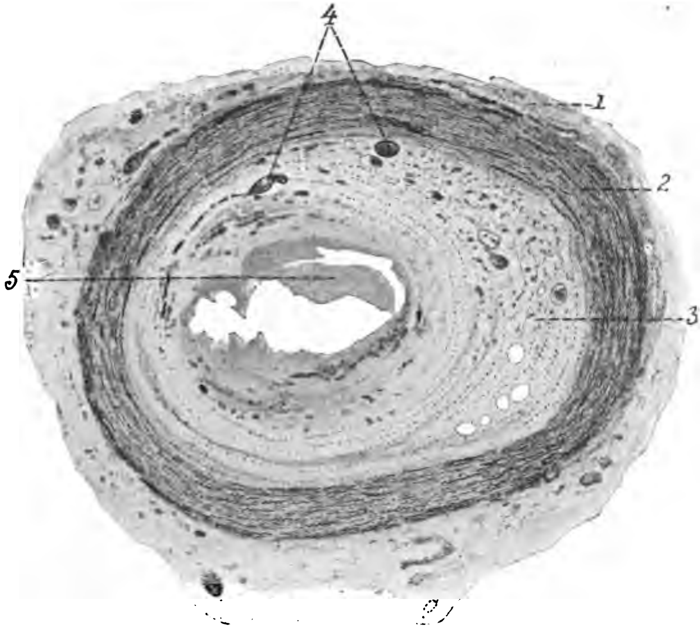


FIG. 3.—ORGANIZED AND PARTLY CANALIZED THROMBUS OF THE BRACHIAL ARTERY (Hemat., Orcein). × 32 (Dürck).

1, Adventitia; 2, tunica media; 3, organized thrombus—*i. e.*, replaced by connective tissue; 4, newly formed and in part dilated vessels within the thrombus; 5, disintegrated remains of the old thrombus.

ried through the circulation and give rise to metastatic abscesses in various parts of the body.

The broken-down portions may become lodged in small vessels, and, acting as emboli, give rise to the condition known as embolism.

Embolism is the intravascular obstruction from the lodgment of a foreign body. The circulating body is known as an *embolus*.

The most common variety of embolus is a dislodged portion of a thrombus, particularly those that occur upon the valves of the heart. Other emboli may be formed by cells of malignant tumors, masses of bacteria, blood parasites, particles of fat, and air.

FIG. 4.—INFECTIOUS EMBOLISM OF THE KIDNEY FOLLOWING ENDOCARDITIS AND SHOWING GROUPS OF STAPHYLOCOCCI IN A GLOMERULUS (Dürck).

The *varieties* of emboli are: (1) *Simple*, *mechanical*, or *aseptic;* (2) *specific*, *infectious*, or *septic*.

The latter is the more severe, as in it suppurative conditions are associated with the mechanical.

Retrograde embolism occurs when, as in whooping-cough, the intrathoracic pressure is increased. An embolus in the inferior vena cava may be carried in a direction opposite to

the blood-current and be thus conveyed into the liver through the hepatic vein.

Crossed or *paradoxical* embolism occurs when the foramen ovale remains patulous. In this condition an embolus may pass directly from the venous to the general circulation without going through the pulmonary vessels.

The results of embolism are numerous:

1. *Inflammation* of the vessel walls is usually the result of the lodgment of the embolus, particularly if it is of the infectious type.

2. *Thrombosis* as a consequence of the stoppage of the flow of blood by the foreign body. The resulting thrombus may be much more extensive than the primary embolus.

3. *Gangrene* may result if the main artery of a part has been obstructed and the collateral circulation has been insufficient or unable to supply the demands.

4. *Necrosis* when the nutrition of a comparatively small area is cut off. Occurs chiefly in the internal organs.

5. *Atrophy* may follow if the blood-supply is not quite enough for the normal demands, but is yet sufficient to prevent actual death of the tissues.

6. *Aneurysmal* dilatation, especially in the brain, sometimes results.

7. *Infarction.*

Infarction.—An *infarct* is the area of degeneration and inflammation produced by embolism in an end-artery. The act of obstruction constitutes infarction.

Infarcts occur only in the so-called end-arteries of Cohnheim—those that terminate in veins or capillaries without anastomosis with an artery. They are found particularly in the kidney, spleen, base of the brain, and lungs, and sometimes in the heart.

The *varieties* of infarcts are: (1) *Anemic* or *white;* (2) *hemorrhagic* or *red.*

The *anemic* occur more commonly in solid organs, such as the kidney; the *hemorrhagic* in organs whose structure is loose, as the lungs. The spleen may be the seat of either form.

An *anemic* infarct is one in which there is an absence of blood.

A *hemorrhagic* one is where the obstructed area is full of blood. It may be the result of a back flow of blood from the veins (Cohnheim's theory), or from free capillary anastomosis. The latter would be particularly apt to occur when the local or general blood-pressure was previously elevated; or when the lodgment of an embolus caused a reflex contraction of the surrounding vessels and thus brought about an overflow of blood into the occluded area through the capillary anastomoses. Another theory is that the blood does not escape until there has been some degeneration of the vessel walls.

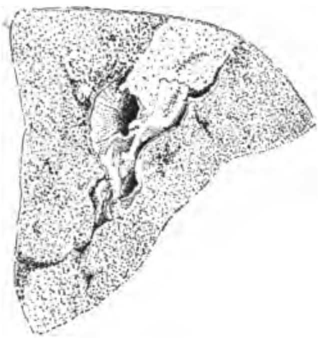


FIG. 5.—IRREGULARLY PYRAMIDAL-SHAPED ANEMIC INFARCT IN THE SPLEEN, WITH SOFTENING ABOUT THE APEX, DUE TO EMBOLISM OF THE SPLENIC ARTERY (Hektoen).

When the blood is cut off a conical shaped area of tissue is deprived of nutrition. As a result, necrosis soon starts in. The apex of this area is directed toward the interior of the organ, the base to the external surface. The base will be swollen and project above the surface of the surrounding tissues.

The infarct is, as a rule, firmer than the rest of the organ, except when it occurs in the central nervous system, where it is usually softer; the firmness depending upon the amount of coagulable material present.

Infarctions of the lung are unusual, as in that organ the capillaries are comparatively large, and the anastomosis between the pulmonary and bronchial arteries may be sufficient to prevent necrosis. To have infarcts occur within the lung that organ must have been the seat of previous disease.

Results.—Infarction is always accompanied by necrosis and fatty degeneration. (1) The tissue may be restored

by absorption and by collateral circulation. (2) It may be replaced by connective tissue with the formation of a scar. (3) It may become encapsulated. (4) Very rarely an infarct may undergo liquefaction necrosis with cyst formation, particularly in the brain.

Edema or **dropsy** is an excess of a clear watery fluid within the tissues between the cells. This fluid differs from the blood-plasma in that it has less albumin, is of a lower specific gravity, is rich in salts, but does not coagulate spontaneously, as it contains very little fibrin. This is called a *transudate* to distinguish it from the fluid present in inflammations, the latter being called an *exudate.*

It is brought about by a disturbed balance between the transudation from the blood-vessels and the absorption by the lymphatics. It may be caused by:

1. *An increased transudation* of fluid from the blood, as in active and passive hyperemia, the latter being the most common form.
2. *Changes in the quality* of the blood.
3. *Increased permeability* of the blood-vessel walls.
4. *Disturbances in the pressure* outside of the vessels.
5. *Obstruction of the lymphatic circulation.*

The most important cause is the alteration of the blood-vessel walls. This condition alone may give rise to marked edema. The changes are dependent upon lack of nutrition.

As a general rule several of the above factors act in combination.

Angioneurotic edema is a localized form due to disturbed innervation.

Edema ex vacuo is that which occurs when an organ does not completely fill its cavity and the remaining space becomes filled with fluid. Usually occurs in the cranial cavity and in the spinal canal.

According to the *seat* of the edema, special terms are employed.

When the subcutaneous tissues are generally involved, it is known as *anasarca. Ascites* refers to a collection of fluid within the abdominal cavity.

Hydrothorax, a collection within the pleural cavities.
Hydropericardium, when within the pericardium.
Hydrocephalus, fluid within the ventricles of the brain.
Hydrocele, when within the tunica vaginalis testis.

The common clinical causes are: (1) Cardiac insufficiency, the edema usually first noticed about the ankles. (2) Kidney disease, first seen about the eyes. (3) Cirrhosis of the liver, accompanied by ascites. (4) Anemia and cachexia. (5) Pressure upon the veins or lymphatics.

Under the microscope the cells of the involved tissues will appear more or less widely separated and in some instances may be vacuolated.

Interstitial emphysema is an infiltration of the tissues by gas. It is usually the result of some injury involving the respiratory tract. It may be due to the presence of some gas-producing bacteria, such as the bacillus of malignant edema or the B. aërogenes capsulatus. It a is comparatively rare condition.

CHAPTER V

RETROGRESSIVE PROCESSES

Aplasia signifies a total failure of development of a part.
Hypoplasia is an incomplete development.

ATROPHY

Atrophy refers to a decrease in the size and in the functional activity of a part. It may be *general* or *local*.

In *general* atrophy the entire body wastes, a condition known as emaciation. It may be the result of lack of food, of starvation, or of disturbances of trophic influences with disorders of metabolism.

In *local* atrophy certain portions undergo changes which may be either *simple* or *degenerative*, or *numerical*, as the latter is sometimes called.

In the simple variety the individual cells undergo a decrease in size.

In the degenerative the number of cells is reduced as a result of disease. This is not considered a condition of true atrophy.

Atrophy may be brought about by there being no longer a demand made upon the part. Through lack of use the cells become smaller.

Old age is often accompanied by atrophy; is seen particularly in the sexual organs.

Pressure is one of the commonest causes; occurs as a result of tight lacing, etc.

Interference with the blood-supply on account of the part not being supplied with a proper amount of nutrition.

Disturbances of the trophic functions, as in poliomyelitis.

The atrophied part will be smaller than normal, and frequently very irregular, causing elevations and depressions.

Microscopically the cells will be reduced in size, more or less degenerated, and frequently pigmented. The latter condition occurs commonly in the heart and is known as *brown atrophy*.

DEGENERATIONS

Degenerations of cells can be divided into two forms:

1. *Infiltrations*, in which abnormal substances are deposited within the cells.
2. *Metamorphoses*, in which the protoplasm of the cell is transformed into abnormal substances.

The changes in the cell may also be either *quantitative*, as when a normal substance is present in an abnormal amount; or *qualitative*, when there is an abnormal substance present.

Necrobiosis refers to the molecular or cellular death of a part.

Parenchymatous Degeneration or Cloudy Swelling.—In it the protoplasm of the cells contains an increased amount of proteid substances. It accompanies very slight disturbances of nutrition, such as occur in inflammation; is found in all infectious diseases and intoxications, possibly as a result of increased bodily temperature, most likely as a result of disturbances of metabolism.

Although all the cells of the body, both glandular and stroma, may undergo this change, they are not equally affected, the glandular ones being more liable to injury. The secreting cells have as their function the removal of certain substances from the body. If the blood contains injurious materials these cells will naturally be the first affected, as they are the more intimately concerned.

This degeneration may follow extensive superficial burns, probably as a result of the action of the poisonous substances absorbed.

Microscopically the individual cells will be swollen and larger, more granular, and more opaque than normal on account of the presence of minute granules. These latter are insoluble in alcohol and ether, but are dissolved by alkalies and weak acetic acid.

The function of the cell is more or less disturbed, but complete recovery frequently occurs. If, however, the cause persists fatty metamorphosis results.

Fatty infiltration is the deposit of fat within the cell or intercellular tissues. May be *general* or *local.* It may occur in cells that normally contain no fat, or else appear in excess in cells that do contain it.

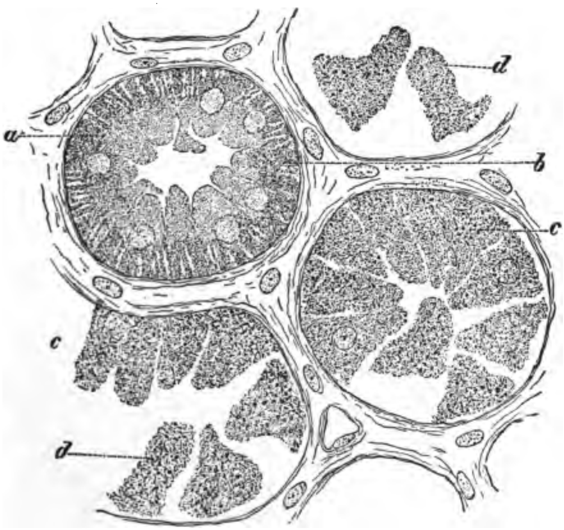


FIG. 6.—CLOUDY SWELLING OF RENAL EPITHELIUM. × 800 (Ziegler). *a*, Normal epithelium; *b*, beginning cloudy swelling; *c*, marked degeneration; *d*, desquamated degenerated epithelium.

The fat contained within the cells is made up of neutral palmitin, olein, and stearin.

Fatty infiltration may be *hereditary*, as obesity in successive generations; may result from *excessive nutrition*, particularly if combined with *lack of exercise.*

The use of *alcohol*, especially in the form of malt liquors.

Anemia, on account of the insufficient oxygenation of the tissues.

In certain *cachectic* conditions, as in phthisis; where the liver is frequently filled with fat.

The most common seats are the subcutaneous and subserous tissues, the omentum and the mesentery, in the liver, heart, kidney, and between the muscle-fibers.

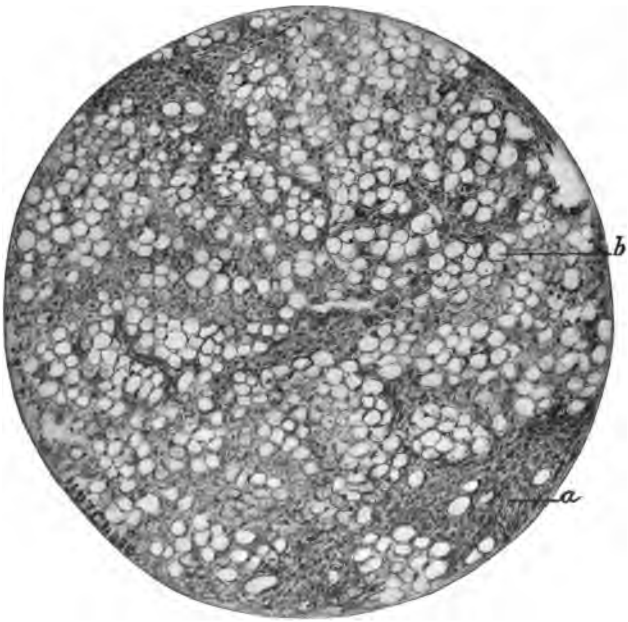


FIG. 7.—FATTY INFILTRATION OF THE LIVER (McFarland). *a*, Periportal connective tissue; *b*, fat drops in liver cells.

Certain other regions, such as the subcutaneous tissue of the penis, nose, ears, lips, and eyelids, are never involved.

An organ the seat of fatty infiltration is larger, paler, mottled, streaked, or diffusely yellow, softer, more friable and greasy on section.

Under the microscope the fat may be found either inside

or outside of the cells. If outside, it is most marked along the fibrous bands.

Inside the cell, particularly the glandular variety, the fat occurs in droplets which tend to enlarge and coalesce. The nucleus is displaced, giving the "signet-ring" appearance, or obscured; is seldom destroyed. The cell wall remains intact.

The *tests* for fat are sudan III, which stains it scarlet, or a 1 per cent. solution of osmic acid, which stains black. It is soluble in alcohol, ether, and xylol; insoluble in water, acids, and alkalies.

Adipocere refers to the transformation of the fats into a wax-like substance most common in bodies that have been buried in damp earth.

Fatty metamorphosis is a conversion of the cell protoplasm into fat.

Generally speaking, the causes of cloudy swelling will bring about fatty degeneration if they are severe enough or act for a sufficiently long time. It occurs in *senility*, particularly when associated with marked arteriosclerosis, in *anemia*, either as a result of hemorrhage or in diseases such as leukemia and pernicious anemia. The condition is probably more widespread in the latter than in any other disease. Occurs also in long-continued and high fever.

The most important substances causing the metamorphosis are the *poisons*, as the metallic salts, chloroform, coal-tar products, etc.; those formed by micro-organismal activity, as in yellow fever.

Organs undergoing this change are generally smaller, paler, and yellowish, soft, flabby, and easily friable; may undergo caseation.

The liver in yellow fever is a typical example.

Microscopically the cell protoplasm contains a large number of minute droplets that rarely coalesce. The nucleus is soon involved and ultimately is destroyed. The entire cell may break down into a fatty granular mass, sometimes called a "compound granule cell."

To distinguish between fatty metamorphosis and fatty infiltration is frequently not only difficult but impossible,

especially so in the liver. The droplets may coalesce in metamorphosis and remain separate in infiltration.

Crystals of margarin and the notched rhombic plates of cholesterin are frequently found in the fatty areas.

Hyaline metamorphosis is a conversion of cells and intercellular substance into hyaline material.

The cells of the connective tissue are most frequently involved, but epithelial and muscle cells may be affected.

The hyaline material occurs in the form of granules and

FIG. 8.—HYALINE DEGENERATION OF AN OVARIAN CAPILLARY. Oc. 2; ob. 9 (McFarland).

is glistening waxy, and with Van Gieson's method stains intensely red.

It is at times scarcely distinguishable from amyloid metamorphosis.

It is found as a result of infectious diseases, septic processes, in chronic intoxications, such as lead poisoning, and in new growths. Its formation is probably dependent upon some malnutrition of the tissues. Generally this form of

degeneration is not sufficiently extensive to be recognized by the naked eye.

The most common site is in the endothelial and subendothelial tissues of the blood-vessels. The lumen will be narrowed or obliterated according to the extent of the thickening of the wall.

It also frequently occurs in the interstitial tissues, as between the renal tubules, between muscle-fibers, hepatic

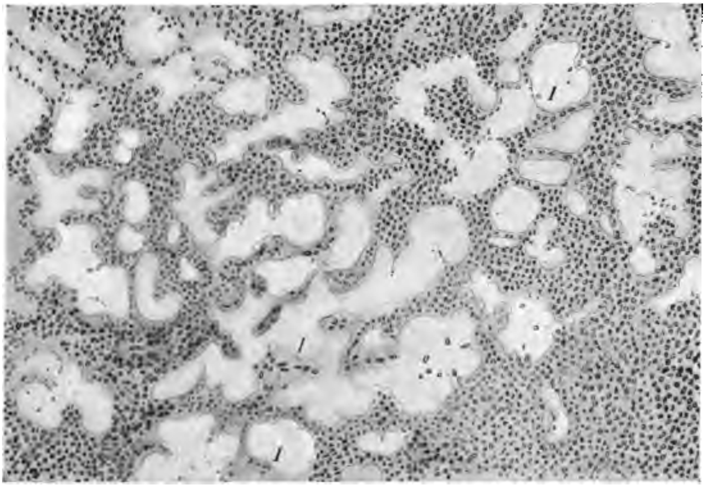


FIG. 9.—HYALINE DEGENERATION OF THE RETICULUM OF A LYMPH-GLAND IN TUBERCULOSIS. × 280 (Dürck).

Among the lymphocytes are seen single reticular fibers, which are greatly thickened and transformed into shining, homogeneous, nonnucleated bars (1).

cells, and in the reticulum of lymph-nodes (Recklinghausen's degeneration). A third site is within the cells, particularly those of mesodermic origin.

It is either formed within the cell or, being formed elsewhere, has been brought to and deposited within the cell.

Mucoid or myxomatous metamorphosis is the conversion of cells and intercellular substances into mucin.

Mucin is insoluble in water but will absorb it; is soluble in alkaline solutions but is precipitated by weak acetic acid.

Either epithelial cells or the intercellular substances may undergo mucoid change. The latter is the more truly a metamorphosis.

It occurs in epithelial cells in all forms of catarrhal inflammation, in the cells of epithelial cysts, and in some carcinomata.

It is found in the interstitial tissues in both epithelial and connective-tissue growths, in some inflammatory conditions, and in myxedema.

The mucous membranes will be covered by a coat of thick, stringy, and viscid exudate. The underlying tissues may or may not show congestion.

Connective tissues will be more or less soft, slightly swollen, and will tear easily. If the condition is very much localized, cysts filled with mucin may be found. Three substances closely related are included under the heading of myxomatous metamorphosis: *mucin*, *pseudomucin*, and *paramucin*, each one differing slightly from the others in its reaction.

The typical mucoid cell is the so-called "goblet-cell" that is found in the large intestine.

The mucoid change looks under the microscope very much like edema. The cells are widely separated and the structure of the tissue is poorly defined. The cells frequently stain poorly and degenerate.

Colloid metamorphosis is the transformation of the cell into a thick, sticky substance known as colloid. It is found only in epithelial cells. It is not precipitated by acetic acid or by alcohol, nor does it swell in water. It usually stains orange color with van Gieson.

It is normally found in the acini of the thyroid gland and in the pituitary body. It is frequently found in parovarian cysts, in goiter, in the tubules of the kidney, in chronic nephritis, and in the prostate gland.

In cysts the colloid material is generally contained in

many small cavities, giving rise to a honeycomb appearance. It may be transparent, yellowish, bluish, or chocolate color, according to other substances present.

Amyloid metamorphosis is a degeneration of the connective tissues into an abnormal substance giving an amyloid reaction. The origin of this material is obscure. It may be formed *in loco* or else brought to the tissue from some other part of the body. It does not exist as such in

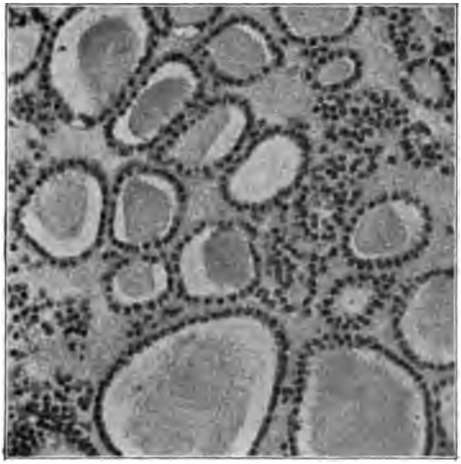


FIG. 10.—COLLOID DEGENERATION OF THE THYROID GLAND, SHOWING MASSES OF COLLOID MATTER IN THE GLAND ACINI (Karg and Schmorl).

the blood, but is very probably derived from substances contained in that fluid. Some believe that the leukocytes, others that the erythrocytes, are the cells from which it is derived.

It is frequently called *waxy*, *lardaceous*, or "*bacony*" disease; is found in the intercellular portions of the connective tissues and not in secreting cells.

It is found as a result of long-continued suppuration and ulceration, such as occur in diseases of the bone, chronic tuberculosis, syphilis, leukemia, and dysentery.

The organs most commonly affected are the kidney, liver and spleen, the larger blood-vessels, the mucous membrane of the intestines, the lymph-nodes, and the heart.

The involved organs are generally pale, larger and firmer than normal, and with rounded edges. The cut surface is smooth, glistening, and transparent, either diffuse or localized. The usual sites of the degeneration are the walls

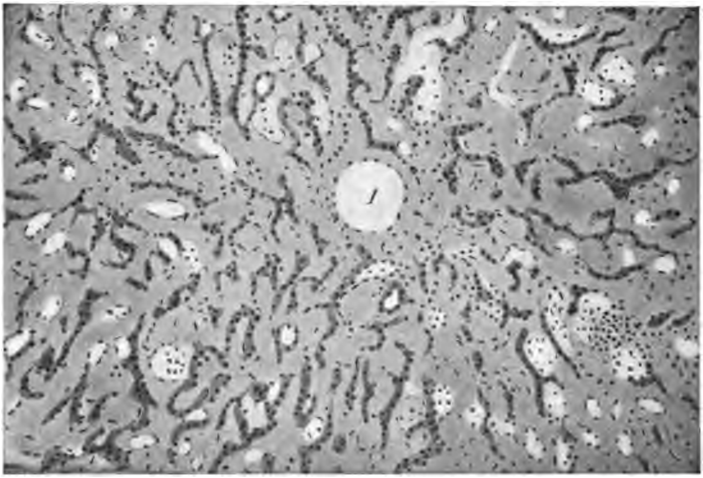


FIG. 11.—AMYLOID DEGENERATION OF THE LIVER. × 98. Hematoxylin-eosin (Dürck).

1, Central vein. Portal capillaries surrounded by homogeneous masses and bands; the epithelial lining distinct. Columns of liver cells compressed to narrow, atrophic strips.

of the capillaries, in the intima and media, the adventitia being rarely affected.

In the kidney the capillaries of the glomeruli are first attacked, converting the bodies into waxy, homogeneous masses; finally the connective tissue may be involved.

In the liver the metamorphosis is deposited between the periportal connective tissue and the central vein. In the

spleen it may give rise to the "sago spleen," a condition which is brought about by the formation of amyloid material in the Malpighian bodies. Later on, the organ may become very extensively involved. In some cases the vessels in the trabeculæ of the organ may be the seat of the metamorphosis.

When amyloid material has been once deposited it is practically never removed. It is insoluble in water, alcohol, ether, dilute acids, alkalies, etc. Unless special staining methods are employed it frequently cannot be distinguished from hyaline degeneration.

When the affected tissue is placed in Lugol's solution (iodin 1, potassium iodid 2, water 100) the amyloid substance becomes a mahogany brown. If stained in 5 per cent. aqueous gentian-violet the amyloid will appear pink, the normal tissues blue.

If after staining in iodin weak sulphuric acid is added, the amyloid will turn blue.

Corpora amylacea or amyloid bodies are found in the prostate gland, in lymphatic nodes, and in the central nervous system. They are concentrically striated like a starch granule, and although in their reaction they may resemble starch and amyloid, they are probably neither.

Glycogenic infiltration is a deposit of glycogen within the cells. It is found normally in small amount throughout the body except in the mammary glands and central nervous system.

It is greatest in amount in the cells of the liver, in voluntary muscles, and in the kidneys; is also present normally in the blood, both in the plasma and in the cells, particularly the polymorphonucelear leukocytes. It is also commonly found in malignant tumors of mesodermic origin (sarcomata).

The origin of the glycogen is not clear; it is a carbohydrate, but seems to be derived from proteid and carbohydrate substances. Glycogen is most frequently found in the condition known as diabetes.

Tissues containing large amounts of glycogen may have

a distinct hyaline appearance. The reactions, however, differ, as it is soluble in water, but not in alcohol, ether, or xylol; is colored a brownish-red on the addition of tincture of iodin 1 part, absolute alcohol 4 parts. The brown is not changed to blue on the addition of sulphuric acid.

Microscopically glycogen occurs in the cells in clear, colorless droplets, usually near the nuclei.

Serous or edematous infiltration is a condition of dropsy of the cells. All kinds of cells may be involved, but it is most common in the epithelial. It is an absorption of an excess of plasma by the cells.

It may accompany general dropsy or result from inflammation; is also found in tumors.

The part involved is usually enlarged, spongy, and edematous.

The cells are distended and filled with large and small vacuoles in the protoplasm and at times within the nucleus.

Pigmentary infiltration is the deposit of pigment within the tissues.

According to their origin, pigments may be divided into four classes:

1. Those derived from outside of the body.
2. Those formed from hemoglobin and its derivatives, the hematogenous pigments.
3. The hepatogenous or biliary pigments.
4. Metabolic pigment; that resulting from cellular activity within the body is known as melanin.

The *hematogenous* pigments are three—*hemoglobin, hemosiderin*, and *hematoidin*.

Hemoglobin is dark red in color, amorphous, contains iron, and is soluble in alcohol, ether, and chloroform. It is recognized chemically by the addition to the suspected fluid of a few drops of a fresh tincture of guaiac and then followed by an ethereal solution of hydrogen dioxid. The mixture, which is at first milky white, turns a deep blue.

If the dried blood is dissolved in normal salt solution, then warmed and evaporated, glacial acetic acid added and warmed, small reddish-brown rhombic plates of hemin appear.

When brought in contact with sulphureted hydrogen, hemoglobin combines and forms ferrous sulphid, which is black.

Hemoglobin is set free from the erythrocytes through hemolysis, either within the vessels or when the blood has escaped into the tissues. The surrounding structures will be diffusely stained. This is commonly seen postmortem, particularly in those parts of the liver that are in contact with the intestines. When it is set free within the vessels during life, it may be deposited within the lymph-nodes, spleen, and kidney, forming pigment metastases.

Hemosiderin is yellowish or brownish in color, amorphous, contains iron, and is insoluble in water, alkalies, alcohol, ether, xylol, and chloroform.

On the addition of potassium ferrocyanid and weak hydrochloric acid it turns blue (Prussian blue reaction).

It occurs in the blood, in cells and intercellular tissues, as a consequence of recent hemorrhages; apparently results from the slow destruction of the erythrocytes.

The granules are taken up by the phagocytes and may be finally removed by them. Cells filled with the granules are frequently found in the sputum in cases of chronic congestion of the lungs.

Hematoidin is a reddish-brown pigment, found in the form of rhombic crystals; does not contain iron, is insoluble in water, alcohol, or ether, but is soluble in chloroform. It is found at the seat of old hemorrhages, and is generally considered a later form of hemosiderin.

The *causes* of hematogenous pigmentation can be divided into local and general.

Local.—Hyperemia, venous stasis, inflammation, hemorrhage.

General.—Hemolysis resulting from animal poisons, bacterial toxins, chemicals. Action of parasites, as in the destruction of the red cells in malaria.

Hepatogenous pigmentation is due to the presence of pigments derived from the bile, *bilirubin*, which is similar to hematoidin, and its oxidation product, *biliverdin*. The bili-

rubin is formed by the hepatic cells from hemoglobin. It is soluble and consequently is taken up by the blood and carried throughout the body, giving rise to the discoloration known as *icterus* or *jaundice*. Both cells and intercellular substances may be diffusely stained, or if the condition is of long standing, greenish-yellow crystals or granules may be found.

The fluids of the body will also be discolored.

The presence of these pigments can be recognized by *Gmelin's* test. Fuming nitric acid will give a play of colors at the point of contact.

This condition may be caused by (1) obstruction to the outflow of bile through the ducts, *obstructive jaundice;* (2) possibly through excessive bile formation resulting from hemolysis, *hematogenous jaundice;* (3) hepatic disorders, as acute yellow atrophy of the liver.

Metabolic pigmentation or *melanosis* is a discoloration of the tissues through the formation of *melanin* by the cells.

The tissues are colored yellow, brown, or black.

Under the microscope melanin occurs as dark granules in the cells and intercellular tissues.

Its chemistry is not well known. It contains sulphur but no iron, is insoluble in water, alcohol, and ether, but soluble in boiling alcohol, acids, and alkalies.

It is found commonly in the *melanotic sarcoma*. It generally tends to destroy the cells in which it is contained, and for some reason such tumors are generally more rapidly metastatic and fatal than the non-pigmented forms.

In *Addison's* disease there is a general bronzing or melanosis of the skin. In many cases this condition seems to follow extensive disease of the adrenals.

In *malaria* some of the hemoglobin is transformed by the parasite into melanin.

Certain *muscular degenerations*, as in "brown atrophy" of the heart. Is questionable whether such granules are true melanin. Various *skin affections*, as freckles, or *lentigo*, *chloasma*, and also in *pigmented moles*.

Extraneous pigmentation results from the introduction

of coloring matters into the body from the outside. The tissues most commonly affected are those of the lungs, giving rise to the condition known as *pneumonokoniosis.*

Anthracosis, or the deposition of coal-dust, is the most frequent, the lung being colored more or less black according to the amount present.

Siderosis results from the inhalation of fine particles of iron.

Chalicosis, caused by the presence of lime in the lungs.

Argyria is a bluish-gray discoloration of the skin resulting from the long-continued use, internally, of nitrate of silver.

Tattoo marks following the introduction of insoluble coloring substances into the skin.

FIG. 12.—BROWN ATROPHY OF THE HEART-MUSCLE IN LONGITUDINAL SECTION (Dürck).

Calcareous infiltration or **calcification** refers to the deposit of earthy salts within the tissues. Usually it is either in the form of the phosphate or carbonate of calcium, but oxalates are generally present as well as magnesium salts.

This process occurs only in those tissues that are either completely destroyed or else undergoing degeneration as a result of imperfect nutrition.

It is commonly seen in the fibrous framework, but may be found within the cells as well. The favorite site is in the connective tissues that have a poor blood-supply, such as cartilage, the walls of blood-vessels, also in old inflam-

matory areas, in regions of degeneration such as infarcts, around foreign bodies, and in tumors. Is sometimes seen in the ganglionic nerve-cells, in the "pearls" of epitheliomata, and in the tumors of the nervous system called *psammoma*, which are made up of masses of salts deposited in the tissues. The most common seat is probably in the arterial system. It is often the sequel of a senile atrophy of the

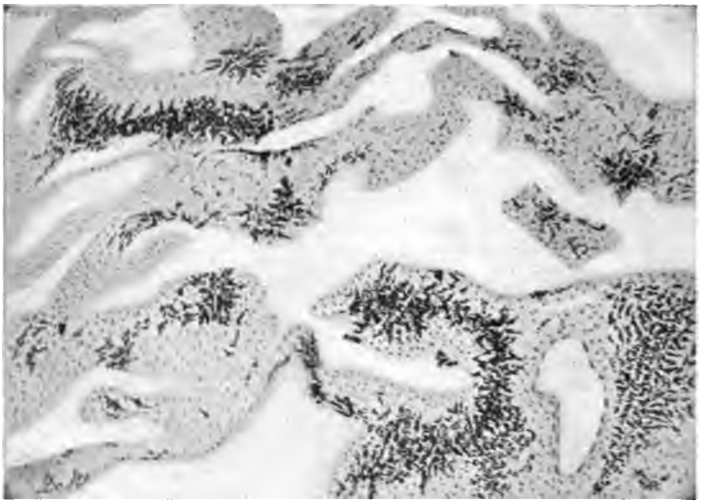


FIG. 13.—ANTHRACOSIS OF THE LUNG. × 100 (Dürck).
The lung tissue is very much indurated as the result of newly formed connective tissue in which are embedded star-shaped masses of fine, granular, blackish pigment of inhaled coal particles.

elastic tissue of the vessel wall along with degeneration of the connective tissue and a general fibrosis.

The valves of the heart frequently undergo calcification, as well as the walls of the aorta, the coronary and cerebral arteries.

Microscopically the salts may appear as granules, spicules, plates or crystals.

If within the cellular protoplasm the granules may be so numerous as to hide the nucleus.

The salts are insoluble in ether but give off carbonic acid gas when dissolved by hydrochloric acid. They also stain very deeply with hematoxylin.

FIG. 14.—CALCAREOUS INFILTRATION OF THE WALL OF A SMALL ARTERY FROM THE WALL OF A GUMMA OF THE LIVER. Zeiss, Oc. 2; ob. D. D. (McFarland).

In addition to the calcification that has occurred in the media contiguous to the fenestrated elastic layer, there is marked syphilitic endarteritis with great reduction in the caliber of the vessel from proliferation of the subendothelial tissue of the intima.

The deposition of the salts is probably due to a lack of oxygen and an increase of carbon dioxid in the tissues, on account of which there is a precipitation of the magnesium and calcium carbonates and phosphates.

Uratic infiltration in the form of sodium biurate occurs

in the cartilages and fibrous tissues in gout. Ordinarily the above salt is soluble in the blood, but under certain constitutional conditions it is deposited as an insoluble salt. These collections are called *tophi* and are found particularly in the joints.

Necrosis is the death of a part of a living organism. It is the death of a part as distinguished from the death of the entire body. The causes of necrosis are (1) *local injury*, (2) *vascular obstruction*, and (3) *trophic disturbances.*

Under the local injuries are included those that are mechanical, chemical, thermal, and bacterial.

Mechanical injuries may cause destruction of the cells directly or by interference with the blood-supply. Pressure of foreign bodies will often bring about necrosis.

Chemical substances such as the acids and alkalies may cause destruction of the tissues.

Thermal injuries, those from extreme heat or cold, will more or less quickly destroy the vitality of the cells.

Bacterial products acting as toxic agents will frequently cause necrosis and gangrene.

If vascular obstruction take place suddenly, the nutrition will be shut off and necrosis result.

Trophic disturbances will lessen the resisting power of the tissues with subsequent necrosis. This is seen in decubitus or bedsore that occurs in various forms of spinal disease. The perforating ulcer of the foot is another example.

The cells in the necrosed areas will show different stages of disintegration. The cell wall may remain, but the cytoplasm will not stain. There may be complete destruction and breaking down of the cell. The granules in the protoplasm disappear and it in turn becomes cloudy, gradually breaks up, and vacuoles form. The nucleus may lose its staining power or may undergo destruction in one of two ways: By *karyorrhexis*, a breaking down of the chromatin into granules, or by *karyolysis*, a liquefaction of the nuclear constituents.

Necrosis may be of different varieties.

Coagulation necrosis is a form of death of the tissues with

a consolidation of the proteid contents. It is a change similar to the coagulation of the blood. The fibrin ferment present acts upon the fibrin factors and fibrin is formed.

It is found in thrombi, blood-clots, and interstitial hemorrhages.

Occurs in various inflammatory exudates, particularly in croupous pneumonia and diphtheria, and in infarcts.

The seat of the necrosis is firmer and paler than normal, and dry. Later on it may become softer and discolored as a result of disintegration of blood.

Caseous necrosis is a condition in which the tissues have been transformed into a cheese-like substance.

It is found only as a sequel to pre-existing coagulation necrosis. Is found most commonly in tuberculosis, but occurs in tumors and in syphilis.

Surrounding the area of caseation there is generally a zone of coagulation.

Liquefaction or *colliquation necrosis* is the death of the tissues with liquefaction. It occurs in those tissues that contain little proteid substance, especially in anemic infarcts of the brain. The nervous tissue undergoes a softening, becomes semifluid, and eventually liquid, remaining as a colliquation cyst.

Gangrene may be of two forms—dry and moist. The tissues involved are those that are exposed either directly or indirectly to the atmosphere.

Dry gangrene or *mummification* is the death of tissues with subsequent drying. It occurs particularly in the extremities of old people or of those who are much debilitated. Is generally due to some obstruction of the arterial system, by a thrombus, an embolus, by disease of the walls, by a spasmodic contraction of the vessel or by pressure from the outside. It is usually circumscribed, there is very little odor, the tissues become almost black and mummify through evaporation of the moisture.

Moist gangrene is the death of living tissues plus an infection by bacteria that are capable of producing putrefaction.

It occurs in those parts that are exposed to the air, either directly or indirectly.

It takes place in people who have previously been in good

FIG. 15.—SENILE DRY GANGRENE OF THE LOWER EXTREMITY, SHOWING LINE OF DEMARCATION (Hektoen).

physical condition, usually as the result of extensive venous obstruction.

The part involved undergoes necrosis and afterward becomes infected. It becomes greenish-black, gas bulbs appear on the skin or in the tissues, and an extremely offensive odor develops.

The cells break down completely, hemorrhage takes place as a result of destruction of the blood-vessels, and many toxic substances are formed. They resemble the alkaloids and may bring about marked disturbances of the organism. This form of gangrene may terminate in several ways.

The dead tissue, *sphacelus* or *slough*, gives rise to a zone of inflammation, which is known as the *line of demarcation*, at the point of contact with the healthy tissue. At this site there is a constantly increasing interval between the dead and living tissue. The tissues here break down and form the *line of ulceration*. It is an attempt of nature to throw off the foreign substance and at the same time to form new tissue. The process is known as *exfoliation*. If the necrotic tissue cannot be thrown off, as is the case when bone is involved, there will probably be a *sequestrum* formed. This is the result of new bone forming around the dead tissue before there has been time for it to exfoliate.

If the degenerated area cannot be discharged, as when the internal organs are involved, it frequently becomes surrounded by a capsule of connective tissue that protects the neighboring parts—process of *encapsulation*. Again, the necrotic tissue may disappear through *absorption*, may *calcify*, or undergo *cicatrization* or *organization*.

Fat necrosis is a peculiar type occurring usually in the fat within the abdominal cavity. In nearly all cases it seems to be dependent upon some disease of the pancreas.

It is the result of the splitting of the fat molecule into its fatty acid and into glycerin. The fatty acids are deposited as crystals and unite with calcium to form salts.

These areas are generally about the size of a pea, whitish in color, soft or gritty. A zone of inflammation may or may not surround them.

Death is the cessation of life. Meaning that all the component parts of the organism cease to live.

Up to a certain time the cells of the body are able to supply all the needs, but eventually the natural term of life is reached and the cells gradually fail to support the tissues. Such a condition would be termed *physiologic* death. If, however, it follows as a result of diseased processes, it would be *pathologic*.

The two, however, cannot be strictly separated, as in old age there are always conditions present that are not normal.

The conditions absolutely necessary for life are a continuation of *circulation*, *respiration*, and *innervation*.

There may be a destruction of certain portions of the body without death following, but a cessation of any of the above-mentioned functions brings about dissolution. This is known as *somatic* death, and according to which function ceased, it is said to have taken place by *syncope*, *asphyxia*, or *coma*.

Molecular death refers to the death of cells.

Signs of death are those that indicate that the organism has ceased to live. Cessation of the necessary functions may give rise to *apparent* death, but without other indications it cannot be diagnosed with certainty.

The necessary signs are:

Algor mortis, a fall of the temperature to that of the surrounding atmosphere. Following tetanus it may, however, be preceded by a distinct rise, continuing for some hours.

Livores mortis or *post-mortem lividity* are the discolored areas that appear in the dependent portions of the body as a result of the dilatation of the blood-vessels. It is often of great importance to distinguish this condition from the discoloration following a blow. In the first the color will disappear on pressure, but in a bruise it will remain, as the blood is not within the vessels.

Rigor mortis or *post-mortem rigidity* is a stiffness due to the coagulation of the albumin of the muscles with the formation of myosinogen. It is first seen in the muscles of the neck and jaws, then extends downward, involving the entire body.

It generally comes on within four to twelve hours, but may

appear immediately or be delayed for twenty-four hours. At the end of twenty-four to forty-eight hours it usually passes off.

If death has occurred suddenly and the individual is in good health, it appears much more quickly than when death has taken place slowly.

Decomposition is the infallible sign. Its appearance depends upon the surrounding temperature, taking place more quickly in hot weather. It is first noticed as a greenish discoloration of the abdominal wall. Is due to the sulphuretted hydrogen from the intestines acting upon the iron contained within the hemoglobin.

The tissues soften, and there is more or less odor, due to the formation of various gases.

Loss of elasticity, *relaxation of the sphincter muscles*, and *loss of transparency of the cornea* and *dilatation of the pupils* complete the list.

Apparent death may occur in hysteria, catalepsy, submersion, cholera, exposure to cold and action of electricity. It is detected by the absence of the signs of true death. The tissues will appear reddish if a light is held behind them, blood will flow from a wound, moisture will collect on a mirror held in front of the face, and the muscles will react to electricity.

CHAPTER VI

INFLAMMATION AND REGENERATION

Inflammation is the protective reaction of tissues to the effects of irritants.

Etiology.—The causes of inflammation may be divided into *mechanical*, *chemical*, and *vital*, or *infectious* and *non-infectious*.

Traumatism of any nature, such as a blow or the action of chemicals, can give rise to an inflammatory reaction and be non-infectious.

The common cause, however, is the action of *bacteria* upon the tissues. The great majority, therefore, of inflammations are infectious or vital in variety.

A non-infectious one may become infectious through a secondary deposit of bacteria.

An infectious inflammation is distinguished by the fact that it is likely to be progressive, is capable of indefinite increase, and may also be transmitted from one individual to another.

Before taking up the pathologic changes of the circulation it will be necessary to first consider the normal differences in the blood-current in arteries, veins, and capillaries.

In *arteries* the stream is not constant; it is regularly intermittent on account of the rhythmic contractions of the heart. It is more rapid than in the veins; the red cells cannot be distinguished at the height of systole, but at the end of the heart's action the current slows sufficiently for them to be seen. The corpuscles occupy the entire lumen, except that at the end of the pulse-wave they momentarily withdraw from the wall of the blood-vessel.

In *veins* the stream is constant and is regular in speed.

Instead of cells and plasma being uniformly mixed there are two zones present: an *axial* or central zone, composed of blood-cells, and a *peripheral* one, made up of the blood-plasma. In this latter there are occasionally a few leukocytes but no erythrocytes found.

In *capillaries* the current is neither constant nor regularly intermittent. It is constant during the flow.

The *changes in the circulation in inflammation* are as follows:

1. A momentary *contraction* of the blood-vessel following the introduction of the irritant. This is followed by:

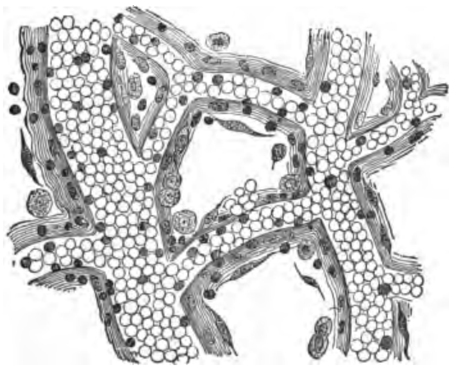


FIG. 16.—INFLAMMATION OF THE MESENTERY, SHOWING OVERFILLING OF THE BLOOD-VESSELS, WITH EMIGRATION OF LEUKOCYTES AND DIAPEDESIS OF RED CORPUSCLES (Ziegler).

2. A marked *dilatation* and *relaxation* of the vessel with at first an increase in the rapidity of the flow. The arterioles are first affected, then the veins and capillaries.

3. Further increase in dilatation with *slowing* of the current. Instead of the cells being unrecognizable in the arteries they now become distinctly visible. Marked changes now occur, particularly in the venous circulation. The plasmatic zone, which at first contained only a few leukocytes, shows an increase in their number until it is entirely filled

with them. Subsequent to this there takes place an exudation of fluid and blood-cells from the vessels.

Emigration or *transmigration of the leukocytes.* At first the leukocytes adhere but slightly to the walls of the blood-vessel, but finally they become closely attached, pass through the walls, and become *pus cells.*

The leukocytes that escape are of the polymorphonuclear variety. They project a small mass of protoplasm through the vessel wall. This mass becomes gradually larger till the cell lies outside in the surrounding tissues. This process is known as emigration.

Diapedesis refers to the escape of red cells from vessels whose walls show no lesions.

At the same time that the cells escape there is an exudation or outflow of lymph through the vessel walls.

As to the emigration of the leukocytes there are various theories, but the reasons are not perfectly understood. The phenomena can hardly be due to nervous influences, as the changes occur too slowly. It is also impossible to bring about an inflammatory reaction by stimulating either the vaso-constrictors or the vaso-dilators. When the latter is done, there is an exudation of plasma but not of cells. According to Cohnheim, there is an increased permeability of the blood-vessel wall due to structural changes.

Probably the chief reason is that the ameboid motion of the leukocytes is very much stimulated.

It may also be the result of *positive chemotaxis*, the attraction that certain substances exert upon motile cells. Dead tissues and the products of bacterial growth are positively chemotactic and their influence may be exerted upon the leukocytes while they are still within the blood-vessel.

Besides the polymorphonuclear leukocyte the round mononuclear form may also escape, giving rise to the *round-cell infiltration* that is found in acute inflammation and also in tuberculosis.

As a result of the disturbances of the circulation there are certain changes in the inflamed part as a whole that are frequently spoken of as the *cardinal symptoms* of inflammation:

Pain or dolor, due probably to the pressure exerted upon the terminal nerve-filaments.

Swelling or tumor, due to the increased amount of blood present and to the exudate within the tissues.

Redness or rubor, due also to the hyperemia.

Heat or calor, the result of two causes, one that more blood is brought to the part, the other that the blood moves more slowly and heat accumulates.

Altered function, or functio læso, may be added to the first four.

The products of inflammation are known as *inflammatory exudates.*

A *serous* exudate is one that is composed of fluid that has escaped from the vessels. It contains very few cells and occurs in very slight inflammations.

This fluid differs from the non-inflammatory transudate in containing a greater amount of albumin, and therefore being of a greater specific gravity.

A *fibrinous* exudate is one in which there is more or less fibrin present. It is formed by the action of fibrin ferment acting upon fibrinogen or fibrin-forming substances in the presence of calcium salts. This ferment is yielded probably to some extent by all the cells of the blood, but particularly by the leukocytes. When they die, the ferment is formed and the fibrinogen is converted into fibrin. When the leukocytes are increased in number, the amount of fibrin is usually greater.

A *purulent* exudate is one in which there is a preponderance of escaped leukocytes. It may be found infiltrating the tissues or in a circumscribed area known as an abscess. This exudate is known as pus.

Pus is an opaque, yellowish, alkaline fluid. It is made up of pus cells, either living or dead polymorphonuclear leukocytes, and *pus serum* (liquor puris). Usually some degenerated tissue cells are present. According to whether there is blood, serum, or mucus as well, it may be *sanious pus*, *sero-pus*, and *muco-pus*.

If the fluid portion is scanty, the pus may be *creamy* or *cheesy;* or *ichorous* if the pus is very thin, watery, and acrid.

An *abscess* is a circumscribed collection of pus. It is surrounded by an inflammatory zone incorrectly called a pyogenic membrane.

An abscess may be *hot* or *cold*. The first is the result of acute inflammatory changes. The latter is a chronic inflammatory process and the fluid contained within it is not pus but is made up of broken-down and degenerated tissues.

An *embolic* abscess is one that has followed the lodgment of a septic embolus.

Pyemic or *metastatic* abscesses are those resulting from pyogenic organisms being present in the blood.

The destruction of tissue that accompanies abscess formation is in consequence of there being an insufficient amount of nutrition and is due also to the dissolving effect of digestive enzymes present in the liquor puris.

When the broken-down tissue has been cast off there remains a superficial lesion with loss of substance. This area is known as an *ulcer*.

A *sinus* is an inflammatory tract that is open at one end from which the exudate can escape.

A *fistula* is an inflammatory tract that is open at both ends. It is one that joins an internal cavity to the surface.

A *hemorrhagic* exudation is one that contains erythrocytes. It generally indicates that there has been a lesion of blood-vessels.

The termination of inflammation depends upon the degree of inflammation and the amount of damage done. It may occur by *resolution*. This takes place only when the inflammation has been slight. The exudate is taken up by the lymphatics and returned to the circulation. Any degenerated cells will be taken up by the wandering leukocytes and the tissue will resume its normal condition.

In *suppuration* the inflammation has been destructive; there is actual loss of tissue, with the formation of pus.

As pus is formed it is either confined as an abscess or else it tends to infiltrate the tissues. In either case the body at-

tempts to get rid of the irritating substance by having it follow along the least resistant paths and letting it escape from the body. This process of extension is known as "burrowing"; it results from the increased pressure due to the presence of the pus and to the digestive powers of the enzymes contained within.

In some cases the pus may quickly escape to the surface of the body and be cast off. It may, however, have to burrow a long distance, as in a psoas abscess, before it can escape.

Sometimes the pus may gain entrance into one of the cavities of the body, as the peritoneum or pleura, and give rise to inflammatory conditions there.

According to the cavity involved, the condition has special names. *Empyema* is pus within a pleural cavity; *pyopericardium* when within the pericardial sac; *pyosalpinx* when a Fallopian tube is involved, etc.

Encapsulation is what takes place when the irritating material cannot be removed from the body. The surrounding tissue cells undergo multiplication and the substance is isolated by the formation of a connective-tissue capsule about it.

Organization is the process of repair by means of which the destroyed areas are filled up by connective tissue. It is not a case of the transformation of the inflammatory products into connective tissue, but is a condition of replacing. This new formation of connective tissue is known as a *cicatrix* or *scar*, the process as *cicatrization.*

The cells present in the repair of inflammation are derived from various sources, and consequently differ among themselves.

The *leukocytes* that form the greatest numbers are derived from the blood and are chiefly of the polymorphonuclear variety.

Lymphocytes both large and small, as well as *eosinophiles* in small numbers, may also be present.

Eosinophile cells are actively ameboid and are able to escape from the blood-vessels. As a rule, they are not present in marked numbers except in certain subacute

or chronic inflammations of the skin or mucous membranes.

The *plasma* cells probably originate within the circulation. They are rather large and contain a pale vesicular nucleus eccentrically placed and a finely granular basophilic protoplasm. These cells are usually most numerous in acute toxic conditions and are supposed to play some part in the formation of connective tissue.

The *mast* cells or *basophilic leukocytes* are large cells containing usually a trilobed vesicular nucleus and large granules in the cytoplasm. They are most common in inflammations of mucous membranes and in the neighborhood of tumors, especially if they have undergone mucoid changes.

The *fibroblasts* or *epithelioid* cells are formed by the proliferation of pre-existing connective-tissue cells.

Giant cells, those containing more than one nucleus, are frequently present. The formation of these cells probably takes place in one of two ways. If a single cell is not sufficiently powerful to remove the offending particle, several may coalesce, and in that way successfully make the attack. They may, however, form through a multiplication of the nuclei without division of the cytoplasm.

In the process of *repair* there is formed what is called *granulation tissue*. In it there is the formation of loops of new capillaries derived from the endothelial lining of pre-existing blood-vessels. The endothelial cell becomes larger, the nucleus divides by mitosis, and two cells are formed. These cells continue dividing until a sprout-like process extending into the surrounding tissue is formed. Adjoining sprouts unite, and although at first solid, finally become hollowed out, thus allowing the circulation to be re-established. At the same time that this is taking place there is a multiplication of the *fixed* connective-tissue cells, which surround and act as a supporting framework to the loops of new-forming capillaries.

In the proliferation of the connective tissue there is first found a small round cell with a round or oval nucleus.

As the tissue becomes older the cells tend to elongate and become spindle-shaped. At first they are very close together, but gradually separate, and the homogeneous intercellular substance becomes fibrillar and supports the cells. Those cells concerned in the formation of the cicatrix are called *fibroblasts.*

In the new-formed tissue there is at first an overproduction of cells and blood-vessels, but eventually it becomes less vascular and cellular. This is brought about to a great extent by the contraction of the cicatrix, which, at first reddish and elevated, finally becomes pale and depressed.

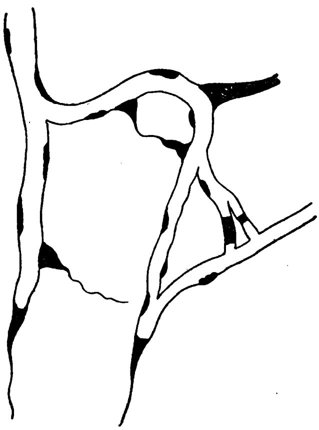


FIG. 17. — FORMATION OF NEW BLOOD-VESSELS, AS SEEN IN THE TAIL OF A TADPOLE (Arnold).

According to surgeons, cicatrization may take place in one of two ways:

Union by first intention, or *primary union.* In this the edges of the wound are closely brought together and very little exudate escapes. In this narrow space the same processes take place as are seen in the formation of granulation tissue, but to a much less extent. The epithelial surface is replaced by a proliferation of the neighboring epithelium.

Union by second intention, *secondary union*, or *union by granulation*, takes place when the edges of the wound are far apart and there is a large amount of exudate present.

This process is the same as healing by first intention, except that in it there is supplied the material to bridge over the gap.

If an epithelial surface is affected, the granulation tissue is gradually covered by proliferation of adjacent cells.

Regeneration, although commonly applied to the formation of cicatricial tissue, really refers to the power of individual tissues to reproduce their own kind.

Generally speaking, the more highly specialized the tissue, the less is its regenerative power. If such tissues are destroyed, they are generally replaced by fibrous tissue. A cell can give rise in regeneration only to a tissue that has the same blastodermic origin.

The *fibrous connective tissue* is probably the most active.

Epithelium of the surface variety is constantly and completely regenerating. Whether regeneration takes place in the more highly specialized epithelial organs, such as the kidney and liver, is rather improbable.

Muscular tissue is capable of regeneration to a slight degree, but the chief repair after injury to muscle takes place within the connective tissues surrounding the fibers.

Blood-vessels, as is seen in the formation of granulation tissue, are capable of marked multiplication. The new-formed vessels in regeneration are usually only temporary; existing only long enough for the tissue to receive its nutrition, then disappearing during the contraction of the cicatrix.

Bone, as is noticed in the repair of fractures, is able to undergo complete regeneration.

Cartilage is incapable of regeneration. In injuries it is replaced by fibrous connective tissue.

Nerve-cells of the highly specialized type, such as ganglion cells, cannot regenerate, but the *neuroglia* or nerve connective tissue can. The neuroglia differs from the ordinary fibrous tissue in that it is derived from the ectodermic layer of the blastoderm.

Varieties of Inflammation.—Inflammation may be,—

Acute when it arises rapidly, lasts a short time, and destroys tissue.

Chronic when arising slowly, lasting a long time, and giving rise to the formation of fibrous connective tissue.

Infectious when caused by some living organism.

Non-infectious when it does not arise from the action of a living organism.

Exudative if the inflammation is characterized by the presence of an exudate. According to the variety of the exudate, the inflammation may be as follows:

Serous when the exudate consists of a fluid having few cellular contents.

Fibrinous when particles of fibrin are present in the exudate.

Purulent when pus cells (leukocytes) are present in large numbers.

Hemorrhagic when erythrocytes escape in quantity.

Parenchymatous when the actively secreting cells of a glandular organ are involved.

Interstitial if the inflammatory process involves the connective-tissue framework of an organ.

Catarrhal when limited to mucous membranes.

Desquamative if there is a casting off of epithelium in a catarrhal inflammation.

In the early stage the secretion of mucus by the cells ceases, the surface becomes dry, and the blood-vessels congested. Later on, the secretion is increased in amount, frequently changed in character, and the congestion of the vessels somewhat lessened.

Vesicular when there are larger and smaller circumscribed elevated areas containing a serous exudate, as in blisters.

Pustular when the circumscribed elevations contain pus.

Diphtheritic or *croupous* when there is a marked coagulation of fibrin on the surface with the formation of a pseudomembrane in which are found degenerated cells of various types—epithelial, leukocytes, and erythrocytes.

In it there is usually necrosis involving the superficial epithelium, or going deeper and attacking the submucosa as well as the mucosa.

Ulcerative if accompanied by a loss of superficial substance.

Degenerative when the destruction of tissue is extensive.

Adhesive when, as the result of the presence of fibrin, transformation into fibrous tissue follows and the two opposing surfaces become more or less adherent. It may go on to the point where the cavity entirely disappears, and is then called *obliterative*.

Gangrenous when there has been infection of the tissues by putrefying organisms and gangrene is present.

Phlegmonous when the interstitial tissues become infiltrated by pus.

Productive when the formation of fibrous connective tissue is prominent.

Specific when caused by a definite micro-organism.

CHAPTER VII

CELL DIVISION

As a result of the tissue injury in disease repair is brought about by cell multiplication or reproduction. The extent of this regeneration depends upon the degree of specialization of the tissue.

The Cell.—The adult cell consists primarily of a mass of *protoplasm* or *cytoplasm* surrounded by a limiting membrane called the *cell wall* and containing a *nucleus* within which there may be a small body called the *nucleolus.*

The *cytoplasm,* which is a semifluid substance, is divided into two portions—the *spongioplasm,* which consists of a very elastic and extensible framework, and the *hyaloplasm,* which is homogeneous and less active.

Imbedded in the cytoplasm are minute granules known as *microsomes.* These are most numerous toward the center of the cell; the peripheral zone, called *exoplasm,* not containing them.

Foreign bodies and vacuolations may also be found within the cell.

The arrangement of the constituents of the cytoplasm varies at different times. Frequently the spongioplasm is arranged as a distinct reticulum. This is, however, not permanent, and seems to depend upon the relative proportion of the hyaloplasm.

The *nucleus* is confined by a distinct wall, the *nuclear membrane,* within which is the nuclear substance or *karyomitome.* This is divided into a framework of fibrils, the *nuclear fibril,* and an interfibrillar substance, the *nuclear matrix.*

The fibrils consist of a part called *chromatin* or *nuclein*

that has a marked [illegible] for nuclear stain. This portion is supported by fine fibrils of *linin* that do not stain.

There is also present a semifluid substance known as the *karyoplasm* or *nuclear juice.*

The *nucleolus* lies within the nucleus and consists of a substance known as *pyrenin.* Just what is its function is not known. It probably [illegible] distinct purpose during cell

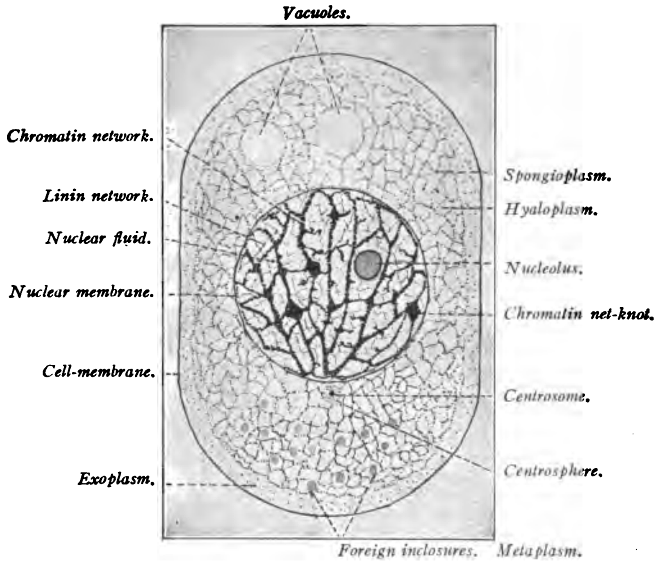


FIG. 18.—DIAGRAM OF A CELL (Huber).

multiplication, as it disappears during the division of the nucleus, but reappears when the new nucleus is formed.

Another body, the *centrosome,* is also sometimes found. It is a small, highly refracting body, situated within the nucleus. It is surrounded by a clear area called the *attraction sphere.* This body, although it may be found during the stage of rest, becomes most noticeable during the stage

of division of the nucleus. At that time it divides into two and passes to opposite poles of the cells.

Occasionally a small irregularly spherical body, the *paranucleus*, is present in the cytoplasm near the nucleus. Its function is not known.

The relation between the size of the nucleus and that of the cell varies greatly. In certain cells, as in the lymphocyte, the nucleus may occupy nearly the entire area.

The nuclei of the same kind of cells are usually similar in shape and size. They may be round, oval, or, as in some of the lower animals particularly, irregular.

A cell may also have one or more nuclei.

With the exception of the red blood-corpuscles and the horny layer of the skin, all cells under normal conditions contain nuclei. The absence of a nucleus, therefore, usually denotes the loss of cellular activity.

The **functions of cells** which distinguish living from inorganic tissues can be divided into:

1. *Metabolism*, the power of selecting and assimilating food, anabolism; and the power of casting off excrementitious matter, catabolism.

2. *Growth*, the result of assimilation producing an increase in the size of the cell.

3. *Irritability*, the response of the living cell to external influences.

4. *Motion*, which may be of three different kinds. There is a constant passage of a "circulating albumin" from one part of the cell to another. It may be *ameboid*, so called on account of its resemblance to the motion of the ameba. It consists of a streaming of the cytoplasm to one point, giving rise to prolongations or *pseudopodia* extending from the surface of the cell.

Ciliary movement is the result of the presence on the surface of cells of minute, hair-like processes, called *cilia*. These are prolongations and specializations of the protoplasm. The cilia keep up a movement like that of a whiplash.

5. *Reproduction* is the multiplication of a cell and may

take place in one of two ways, either by direct division, *amitosis*, which is not the common method, or by indirect division, *karyokinesis*, *karyomitosis*, or *mitosis*. The latter is the more usual way.

In *amitosis* or direct division there is first noticed a slight contraction in the nucleus of the cell. This gradually goes on until two new nuclei are formed. During this period the cytoplasm begins dividing, and by the time the nuclei have migrated to opposite poles, separation has taken place and two new cells have formed.

If the cytoplasm fails to divide, multinuclear or giant cells may arise.

Karyokinesis.—In *karyokinesis*, or indirect division, the cell goes through a very complicated course of changes of the various elements, probably the result of definite metabolic processes.

The changes can best be considered under four headings:

1. *The Prophase.*—The centrosome increases in size, passes from the nucleus into the cytoplasm, and divides into two.

Surrounding each centrosome is a mass of fine radiating lines known as the amphiaster. The rays extending from one centrosome to another are arranged in spindle form, the centrosomes being situated at the apices of the spindles. These achromatin rays form the nuclear spindle.

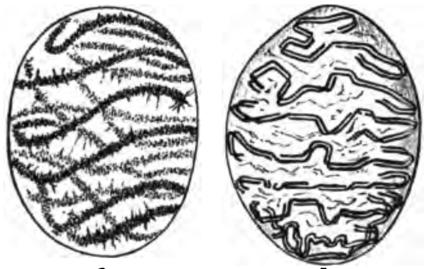
The nucleus has been enlarging and the chromatin increasing. These fibrils become tangled and convoluted and form the *close skein.* The fibrils become thicker, less convoluted, and arrange themselves in irregular loops, forming the *loose skein.* These loops finally separate at their peripheral ends and form the *chromosomes*, V-shaped fibrils with their closed ends arranged in a clear space known as the *polar field.*

During the formation of the skeins the nuclear membrane disappears and the chromatin fibrils lie in the cell protoplasm.

The chromosomes are always present in the same number in the same species, varying from 2 to 36 in various animals; in man being constantly 16.

The arrangement of the fibrils about the polar field constitutes the *mother star* or *monaster*.

2. *The Metaphase.*—Each of the chromosomes under-



a *b*

FIG. 19.—NUCLEAR CHANGES IN KARYOKINESIS (Hatschek).
a, Nucleus of spermatoblast of Salamandra maculata, with chromatin threads forming the first suggestion of a coil; *b*, close coil with disappearance of the fuzzy aspect and longitudinal cleavage of the threads.

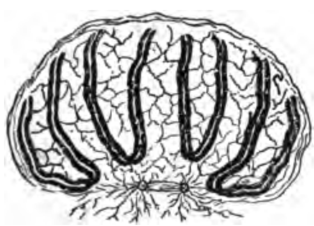


FIG. 20.—DIAGRAMMATIC APPEARANCE OF THE RELATION OF THE CHROMOSOMES TO THE CENTROSOMES AND PRIMITIVE NUCLEAR SPINDLE (Flemming).

FIG. 21.—DIAGRAMMATIC REPRESENTATION OF THE NUCLEAR SPINDLE AND OF THE ARRANGEMENT OF THE DOUBLE CHROMOSOMES IN AN EQUATORIAL PLANE PREPARATORY TO SEPARATION. THIS STAGE IS CALLED THE MOTHER STAR (Flemming).

goes a longitudinal division into two. These filaments, with the closed end advancing, begin to separate, moving toward their respective poles or centrosomes.

3. The *anaphase* begins with the migration of the chromosomes. As they move toward the opposite poles the free

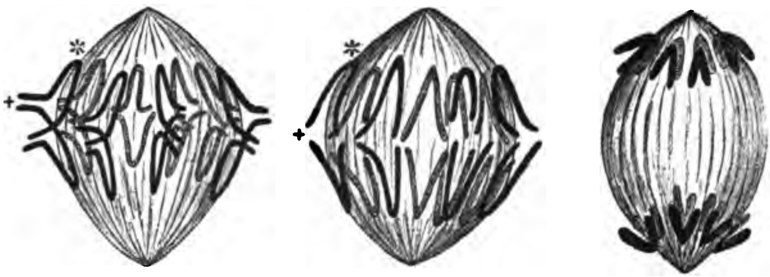


FIG. 22.—DIAGRAMMATIC REPRESENTATION OF THE SEPARATION OF THE CHROMOSOMES, WHICH ARE ATTRACTED TOWARD OPPOSITE POLES OF THE NUCLEAR SPINDLE, ABOUT WHICH THEY GATHER TO FORM THE "DAUGHTER STARS" (Flemming).

ends constitute the *equatorial plate.* Connecting the ends are fine threads of achromatin known as the connecting filaments. The chromosomes collect at the opposite ends and form the *daughter stars* or *diasters.* As this occurs there is the beginning of a constriction of the protoplasm.

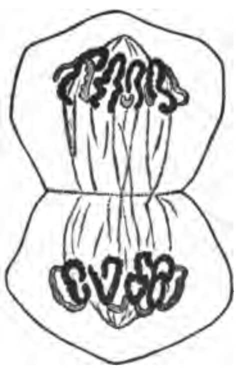


FIG. 23.—SEGMENTATION OF THE CYTOPLASM, AND THE CHROMOSOMES EQUALLY DIVIDED, ABOUT TO FORM NEW NUCLEI IN THE NEW CELLS (Flemming).

4. *The Telophase.*—The constriction continues until the original cell has been completely divided and two new ones formed. The chromosomes now undergo in reverse order the phases that have been described: the loose skein, the close skein, the reappearance of the nuclear membrane and of the nucleolus, with finally the stage of rest.

To summarize, the changes are as follows:

Resting mother nucleus.

Prophase.

Migration and division of centrosome with increase of chromatin.

Close skein.

Disappearance of nuclear membrane.

Disappearance of nucleolus.

Loose skein.

Separation of skein into chromosomes.

Appearance of polar field.

Rearrangement of chromosomes around polar field.

Monaster, or mother star.

Appearance of nuclear spindle.

Metaphase.

Longitudinal division of the chromosomes.

Anaphase.

Migration of the divided chromosomes to opposite ends of the cell.

Formation of the equatorial plate.

Daughter star, or diaster.

Telophase.

Construction of the protoplasm.

Daughter skeins undergoing in reverse order the above changes.

The stage of rest.

In some instances, instead of the cytoplasm dividing when cleavage of the nucleus is completed it remains unchanged. This may go on until there are many nuclei imbedded within a single mass of cytoplasm. Such formations are known as *giant cells* and may be the result of division under unfavorable circumstances.

There may be the formation of more than two centrosomes with a resulting multipolar cell. The equatorial segments may split up more than once and the daughter cells may divide secondarily.

CHAPTER VIII

PROGRESSIVE TISSUE CHANGES

HYPERTROPHY

Hypertrophy, generally speaking, means an enlargement or overgrowth of any kind. It is usually divided into *true* and *false* hypertrophy or *hyperplasia*, as the latter is called.

True hypertrophy is a uniform enlargement of a part, dependent upon an increase in size of all of its component elements. Accompanying the enlargement there is an increase in the functional power of the part involved.

The hypertrophy may be either *congenital* or *acquired*. It may also be either *physiologic* or *pathologic*. The former, however, may come under the latter heading when it reaches a degree that is not normal to the individual.

Hypertrophy is called *compensatory* when one organ takes upon itself the amount of work that was primarily carried on by two; is known as *vicarious* when another function increases at the expense of one that has been destroyed.

Etiology.—1. *Congenital causes*, in which case there are marked overgrowths of portions of the body, especially of the fingers and toes.

2. *Exercise* calls for an increased amount of energy. This demand is met by a greater supply of food with a subsequent increase in size, and is seen in the enlarged muscles of a blacksmith, or in a kidney when the other one is diseased or absent. These are examples of *compensatory* hypertrophy.

3. *Nervous influences* in some indefinite way play a part in hypertrophy, as is seen in the enlargement and increased function of the mammary glands during pregnancy.

4. *Disease of the hypophysis cerebri* apparently causes the condition called *acromegaly*, in which the tissues of the face and extremities hypertrophy.

Morbid Anatomy.—The part affected is uniformly increased in size.

Microscopically hypertrophy may be divided into the *simple* or *true* and the *numerical* (hyperplasia).

In the *simple* there is an increase in the size of the individual cell. This is seen particularly in the pregnant uterus, where at term the unstriped muscle cells may be eleven times as long and four times as broad as normal.

In the *numerical* variety the cells increase in number, but not necessarily in size; may even be smaller than normal.

Hyperplasia, or **false hypertrophy,** is a condition in which there is an increase in number of the cells with usually an asymmetric enlargement of the tissue.

It occurs most commonly in the fibrous connective tissue.

Etiology.—1. *Irritation* is the most common cause, if not too severe in character. In that case inflammation with consequent degeneration results.

The irritation may be *mechanical*, such as results from intermittent pressure exerted by tight shoes, or from the presence of a foreign body. *Chemical* irritants, such as alcohol, will bring about an increase in the amount of connective tissue, particularly in the liver. In which case there is also an increase in the number of bile capillaries.

2. *Nervous influences*, such as bring about the condition known as pseudo-hypertrophic muscular paralysis. In it there is not an increase in the muscle itself, but the fat has undergone a hyperplasia.

3. *Compensatory*, such as occurs when, on account of the decrease in size of an organ, the surrounding tissues have undergone a hyperplasia in order to supply the deficiency.

Morbid Anatomy.—The part involved may be much larger than normal, or on account of the contraction of the newly formed connective tissue, be much smaller. In either case the change is not symmetric.

In elephantiasis the part involved will be large on account of the increase in cells, but it will be very irregular.

In hyperplasia of the connective tissue of the liver the organ may be smaller than normal and have a roughly granular surface.

Metaplasia refers to the transformation of one tissue into one of another variety. The new variety must, however, be one derived from the same blastodermic layer. Epithelium can never be transformed into a connective-tissue type nor vice versa. The term is practically limited to the connective-tissue group. It is seen in the formation of fat from areolar tissue, of bone from fibrous tissue, etc.

Heteroplasia is the development of a new tissue in a locality where it is not normally found. This is seen particularly in connection with neoplasms.

CHAPTER IX

TUMORS OR NEOPLASMS

A *tumor* is a functionless new growth, atypical in structure and frequently harmful to the individual.

The cause of such growths is as yet unknown. They are made up of tissues that have their counterpart either in the embryonal or adult development. They differ in having a more or less atypical arrangement, in occurring in tissues in which they are heterologous, and in not having any mechanism to control their growth and function.

Theories of Origin.—They are numerous, but as yet no one answers in every case.

1. *Spermatic Influence.*—It was thought that the normal tissue where the growth occurred had become directly transformed into the tissue of the tumor, but this is not in any way supported.

2. *Mechanical Irritation Theory of Virchow.*—By this it is claimed that new growths arise in tissues that have been the seat of injury or chronic irritation. Such cases as the development of epitheliomata on the lower lips of pipe-smokers, carcinoma of the gall-bladder associated with gall-stones, scrotal cancer in chimney-sweeps, etc., would seem to uphold this theory. It is probable, however, that the injuries and irritation are not the causative, but are secondary factors.

3. *Theory of Embryonic Remnants* (Cohnheim).—The author of this theory believed that "in an early stage of embryonic development more cells were produced than were required for the formation of the tissue involved, so that there remained unused a number of cells, possibly very few, which, on account of their embryonic character, were endowed with the power of marked proliferation." These

remnants are frequently spoken of as "rests." Cohnheim thought that they could lie latent for many years and develop in after life if conditions should become favorable.

Although these "rests" have never been discovered, yet in certain forms of tumors this theory seems to hold good: in enchondromata of the testis and parotid glands and of other organs, and particularly in the case of the dermoid cysts.

4. *Parasitic or Infective Theory.*—Many investigators have claimed, especially concerning the carcinomata and sarcomata, that tumors are caused by the presence of living micro-organisms. Bacteria were first supposed to be the cause. Later, small round bodies, known as "Russell's bodies," were found in cancer cells and were thought to be protozoa.

Plimmer more recently believed the cellular inclusions to be blastomycetes.

Cultivation of these bodies has generally failed and the result of transplantations of portions of tumors has not been satisfactory.

Many believe the inclusions to be portions of degenerated nuclei or secretions of the cells.

5. *Theory of Decreased Tissue Resistance.*—Ribbert's theory is that the connective tissue loses its normal resisting power, or "tissue tension," and by doing so allows the epithelial cells to undergo abnormal proliferation.

6. *Nervous Theory.*—This was to the effect that through disturbances of the trophic nerves the tissues were able to undergo an overgrowth.

Predisposing Causes.—*Age.*—Certain tumors apparently bear a distinct relationship to the age of the individual. Before thirty years the sarcomata are most likely to appear; after that period, the carcinomata.

Sex.—Women are much more predisposed to tumor formation than are men.

Heredity seems to have some influence, as it has been found that carcinomata are more common in some families than in others.

Occupation, as in chimney-sweepers and in paraffin-workers, who seem to frequently suffer from carcinoma.

Morphology.—Tumors may differ greatly in the following respects:

Size.—They may be of any size, from microscopic to weighing 275 pounds, as reported by Delameter.

Shape.—According to their shape tumors are called *nodular* when spherical, *tubercles* when projecting as a rounded body above the surface of an organ, *flat* or *tabular* when rising as a comparatively level elevation.

When the growth is connected to its original site by a stalk or pedicle it is called a *polyp*. When the surface is very roughened and irregular the tumor may be termed a *cauliflower* or *dendritic* growth.

If like a mushroom with a narrow stalk and a broad head, is termed a *fungus.*

Color.—The color of a growth depends upon the nature of the tissue of which it is composed and upon the amount of blood present. It may also be modified if degenerative processes have taken place.

Consistency depends upon the structure of the growth. If of bone the tumor will be very hard; if of mucous tissue, very soft.

Number.—Tumors may be *single* or *multiple*, there being usually a single *primary* tumor with several *secondary* ones if the growth is malignant. There may, however, be hundreds of primary tumors, as in cases of fibroma molluscum.

A *recurrent* tumor is one that recurs at the place from which it was removed.

According to the arrangement, tumors may be *typical*, *homoplastic*, or *homologous* when they resemble the tissue from which they arise; *atypical*, *heteroplastic*, or *heterologous* when they differ.

If made up of a simple tissue they are called *histoid* tumors; if of a combination, attempting the formation of an organ, *organoid;* and when containing portions of all three blastodermic layers, *teratoid.*

The blood-vessels, which always originate from pre-existing vessels, may be greatly increased in number, *telangiectatic;* in size, *cavernous;* or unusually arranged, *plexiform.* They may be greatly decreased in number, thereby favoring secondary changes, or their walls may be imperfectly formed, giving rise to hemorrhages. Lymphatics are usually present, but the nervous supply is very poor, as a rule.

The *growth* of a tumor is independent of that of the individual. It may continue even if the normal tissues are being sacrificed for it. A lipoma will grow although the patient may not be getting sufficient nourishment to carry on the normal functions of the body.

It may be either *central expansion*, as is the case in benign growths, or *peripheral infiltration*, as in the malignant forms. The latter also increase by means of the central expansion.

As the blood-supply of tumors is usually poor, they frequently undergo various forms of degeneration, as *pigmentation*, *calcification*, *fatty*, *hyaline*, *colloid*, and *mucoid* metamorphoses; *necrosis* and *ulceration.*

According to their effect upon the individual a new growth may be either *benign* or *malignant.*

Benign growths do not affect the patient except as they may press upon vital structures or undergo degenerative processes.

They are usually circumscribed, encapsulated, do not give metastases, and do not recur after excision.

Malignant tumors are those that through their own influences tend to bring about the death of the individual. They are not circumscribed, nor encapsulated, cause cachexia, give metastasis, and recur after excision.

Metastasis refers to the extension of the primary growth by the transference of malignant cells to other parts of the body. It may take place either through lymphatics, as in the carcinomata, or through the blood, as in the sarcomata.

Death may be caused by tumors—

1. *Pressing* upon vital organs.
2. *Invading* vital organs and causing degeneration.
3. *Hemorrhage* resulting from ulceration and degeneration.

4. *Absorption* of poisonous products.
5. *Secondary infection.*
6. *Exhaustion* due to the tumor using up so much nutrition for its own benefit.

Combinations of tumors that have been derived from the same blastodermic layer frequently occur, as fibrosarcoma, etc. One type cannot, however, be transformed into another.

Classification of Tumors.—The simplest is as follows:

I. HISTOID.

Simple Connective-tissue Tumors.

	Atypical.	*Typical.*
Embryonic type	Sarcoma.	Connective tissue.
Adult type	Fibroma { Hard. Soft.	Connective tissue.
	Lipoma.	Fatty tissue.
	Myxoma.	Mucous tissue.
	Chondroma.	Cartilage.
	Osteoma.	Bone.
	Glioma.	Neuroglia.

Specialized Connective-tissue Tumors.

Myoma { Rhabdo-	Striated muscle.
Myoma { Leio-	Non-striated muscle.
Hemangioma	Blood-vessels.
Lymphangioma	Lymph-vessels.
Lymphadenoma	Lymphatic tissue.
Lymphoma	Lymphatic tissue.

Type of Endothelium.

Endothelioma.

II. ORGANOID.—*Epithelial Tumors.*

Neuroma	Nerve tissue.
Squamous epithelioma	Squamous epithelium.
Hard papilloma	Squamous epithelium.
Soft papilloma	Columnar epithelium.
Cylindric epithelioma	Columnar epithelium.
Adenoma } Hypernephroma }	Normal glandular type of cells.
Carcinoma	Atypical glandular cells.

III. Teratoid.—*Mixed Tumors.*

Dermoids.
Teratoma.
Cholesteatoma.

IV. Syncytioma Malignum.—*Chorio-epithelioma.*—Probably belongs under the epithelial tumors.

TUMORS OF EMBRYONAL CONNECTIVE TISSUE

SARCOMA

A *sarcoma* is a tumor made up of cells that resemble those found in embryonal connective tissues. They are characterized by the preponderance of the cells over the intercellular substance, which may be granular, fibrillary, or reticular. The sarcoma cells are not truly embryonal, as they never continue to a complete development. They arise from the mesoblastic layer and often retain the characteristics of the tissue from which they arise, periosteal sarcomata sometimes containing bone.

The sarcomata are essentially malignant; that is, they infiltrate the surrounding tissues, give metastasis, cause cachexia, and return after excision. It is only occasionally that they are encapsulated.

The blood-vessels are generally few in number and imperfectly formed, the single layer of endothelium being supported by a very few connective-tissue fibers. In many cases the blood-channels are simply spaces whose walls are formed by the tumor cells. The imperfect vessel wall explains why hemorrhage in these tumors is so common and why *metastasis* takes place by means of the blood.

Sometimes the blood-spaces may be very large and numerous, thus forming the angiosarcoma.

As a rule, no lymphatics are present.

Sarcomata may occur in any part of the body; as a rule, they are seldom primary within organs.

They generally occur before the age of thirty. Are frequently rounded in shape, somewhat lobulated, and to a certain degree circumscribed. Are hard or soft accord-

ing to the amount of intercellular substance present, or to the variety of the tissue of which they are composed.

Their color is generally pink or grayish; this, however, depends to a great extent upon the condition and number of the blood-vessels.

On account of the poor blood-supply, degenerations, particularly *myxomatous*, frequently take place.

If there is pigment present, either melanin or hemosiderin, the tumor is called a *pigmented* one.

These tumors vary greatly in their malignancy, the small round-cell type, especially if melanotic, being rapidly fatal. The greater the amount of cellular elements, the greater is the malignancy.

The varieties of the tumors depend upon the kind of cell that predominates.

Round-cell sarcomata are those made up of either *large* or *small* round cells.

In the *small*-cell variety the intercellular substance is very scanty. They are rather soft, whitish in color, friable, and a milky juice can be scraped from the cut surface.

They grow rapidly, infiltrate the surrounding tissues, give extensive metastasis, recur quickly after removal, and soon cause death. They may occur in any part of the body and at any age.

The individual cells have large vesicular nuclei and comparatively little protoplasm.

If there is a close resemblance to the arrangement of a lymph-node, small round cells with a distinct reticulum, the tumor is called a *lymphosarcoma*.

The *large round-cell sarcoma* is very similar to the small, but is firmer on account of the intercellular connective tissue present. The cells are larger, and although generally round, may be polygonal, and are sometimes arranged in alveoli.

Are less malignant than the small.

Spindle-cell sarcoma is one that is made up of spindle cells, either large or small. Is one of the commonest forms.

These tumors are quite firm, white, and very little juice

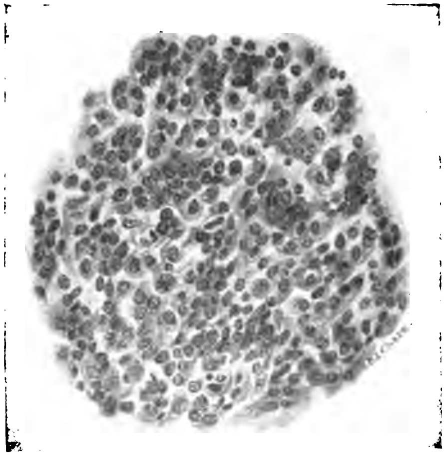


FIG. 24.—SMALL ROUND-CELL SARCOMA OF THE LOWER JAW. Oc. 3; ob. D. D. (McFarland).

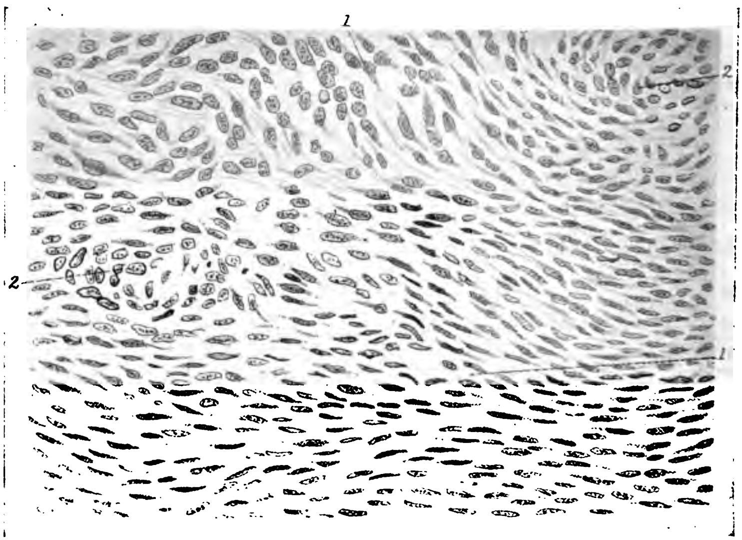


FIG. 25.—SPINDLE-CELL SARCOMA FROM THE BRAIN. Hemat.-eosin. × 300 (Dürck).

1, Spindle-cells cut longitudinally; 2, spindle-cells in transverse section.

can be scraped from the cut surface. The cells are arranged in irregular bundles and have oval vesicular nuclei. The amount of intercellular tissue may be very great, making the tumor quite hard; is then known as a *fibrosarcoma.* It is often difficult to determine whether the tumor is a sarcoma or a fibroma.

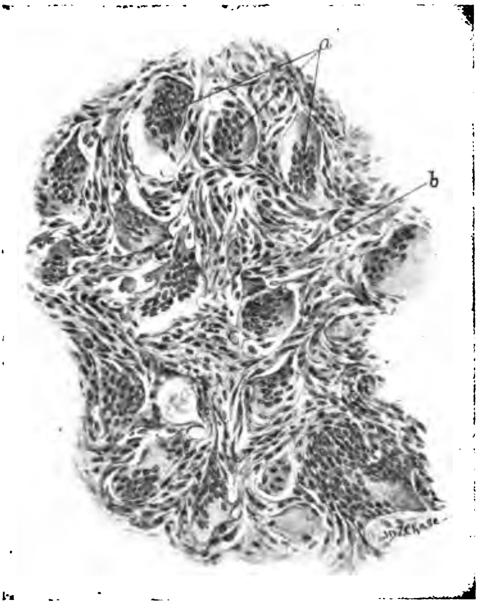


FIG. 26.—GIANT-CELL SARCOMA OF THE THIGH (McFarland)
a, Giant cells; *b*, spindle cells.

The spindle-cell sarcomas are relatively benign; they frequently do not give metastasis, although recurring after removal.

Giant-cell sarcoma is one in which there are found cells made up of a large amount of cytoplasm in which are numerous oval nuclei centrally located. The predominating

cells may be round or spindle-shaped. They are most commonly found in relation with bone and periosteum.

This form is the least malignant of all the sarcomata.

Special names have been given to other forms of sarcoma on account of some special feature.

Alveolar sarcoma is where either groups of round or spin-

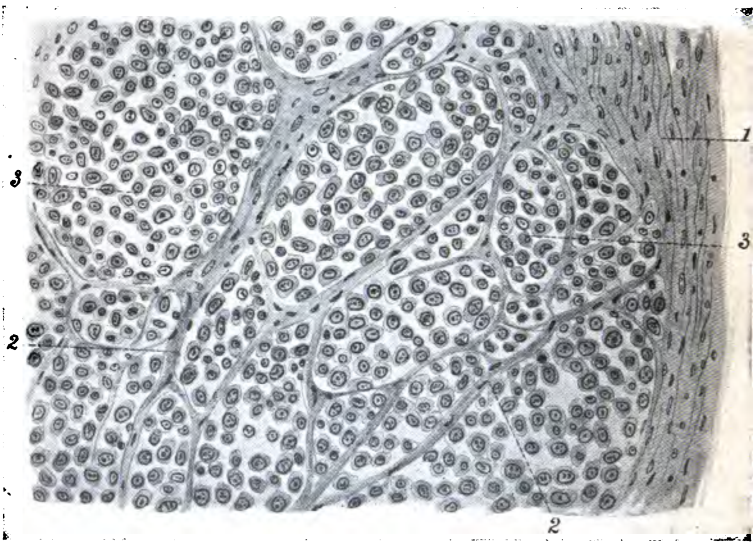


FIG. 27.—ALVEOLAR LARGE ROUND-CELLED SARCOMA FROM THE PERIOSTEUM. Hemat.-eosin. × 250 (Dürck).

1, Heavy septum of connective tissue; 2, delicate connective-tissue reticulum: 3, polyhedral cells with vesicular nuclei.

dle cells are surrounded by distinct bands of connective tissue.

Melanotic sarcoma is one of any type in which there is *melanin* present. This pigment may be found either in the cells or in the intercellular tissue.

They occur in the skin, the choroid coat of the eye, and in the ciliary body.

Are very malignant, give widespread metastasis, and rapidly prove fatal. The liver is the common secondary seat for primary melanotic sarcoma of the eye.

Myxosarcoma is one in which there is a marked mucoid degeneration present.

Angiosarcoma is a growth that contains many blood-vessels. If the walls of these vessels or the neighboring

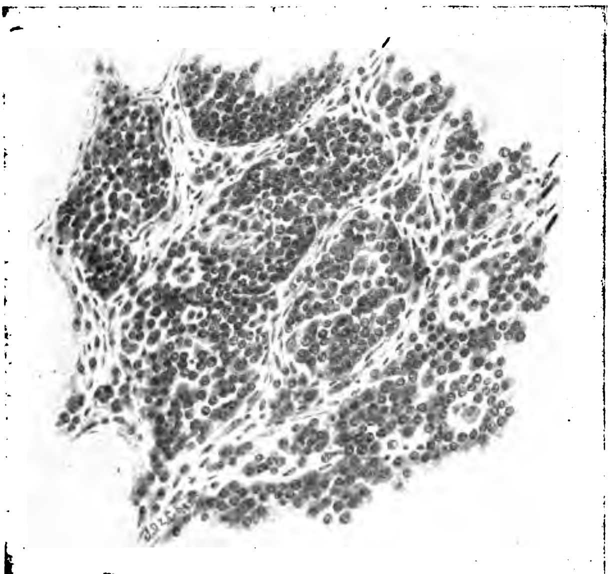


FIG. 28.—ALVEOLAR SMALL ROUND-CELL SARCOMA. Zeiss, Oc. 4; ob. c. (McFarland).

cells undergo a hyaline degeneration, the sarcoma is spoken of as a *cylindroma*.

If the tissue with the exception of those cells in the immediate neighborhood of the vessels undergoes a mucoid change, the growth is called a *myxangiosarcoma tubulare* or *perithelioma*.

Chloroma is a variety of sarcoma arising from the periosteum; is greenish in color.

Psammoma is a tumor allied to the sarcoma. It is made up of masses of spindle cells, which contain areas of hyaline degeneration and calcification. Are usually found in the meninges of the brain and spinal cord.

Endothelioma is a tumor arising from endothelial cells. These growths are at times very difficult to differentiate from carcinoma on account of the apparent cell nest arrangement.

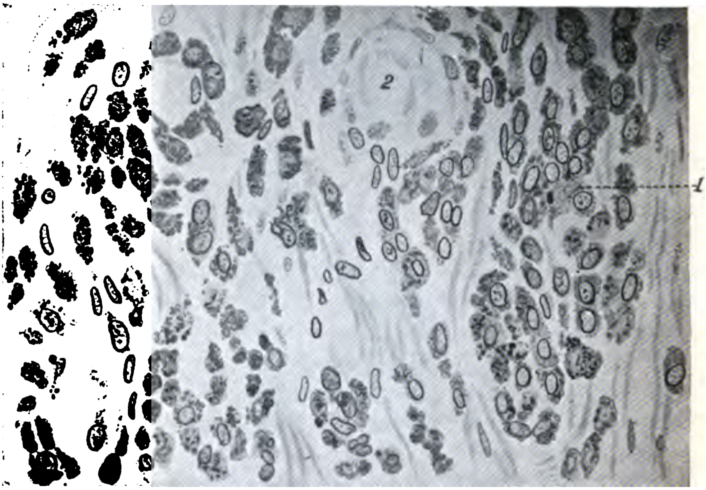


FIG. 29.—METASTATIC MELANOSARCOMA OF THE PERITONEUM. Hemat.-eosin. × 320 (Dürck).

1, Nests of darkly pigmented polygonal cells; 2, cross-section of vessels.

The cells extend along the lymphatic spaces and are closely related to connective tissue. Are found in the serous membranes, testicle, ovary, and liver. Are malignant.

According to the combination of tissues present, the following varieties will be only mentioned:

Osteosarcoma	=	bone present.
Chondrosarcoma	=	cartilage present.
Myosarcoma	=	muscle present.
Neurosarcoma	=	nerves present.

TUMORS OF ADULT CONNECTIVE TISSUE

Fibroma is a tumor of fibrous connective tissue. Fibromata are usually pale in color, round, lobulated, circumscribed, and encapsulated. They may be of varying degrees of firmness.

FIG. 30.—PERITHELIOMA OF THE RETINA (McFarland).
a, Blood-vessels surrounded by cells in a good state of preservation; *b*, degenerated portion of tumor.

The cells resemble those of normal connective tissue and are arranged in bundles that cross each other in all directions.

FIG. 31.—ENDOTHELIOMA OF THE PLEURA. (Zeiss, Oc. 2; ob. c.) (McFarland).

The illustration shows the cellular growth in the form of cylindric masses which fill crevices of the tissue, probably originally lymphatic channels.

FIG. 32.—.HARD FIBROMA (Warren).

In the *soft* variety the cells are separated by serous or mucous deposits.

In the *hard* the cells are closely packed together.

Fibromata are benign and frequently undergo various degenerations. Occur in all parts of the body, particularly in the uterus, where they attain great size. In this locality are usually combined with muscle tissue, forming the *fibromyomata.*

They may occur in combination with sarcoma, or any of the various forms of adult connective tissue, as fibrolipoma, myxoma, chondroma, etc.

A *keloid* is a fibrous tumor that forms usually from a scar. It is not confined to the seat of the original injury, but extends somewhat into the surrounding tissues. Is usually smooth, and is most frequently seen in negroes.

Molluscum fibrosum is a condition in which there are numerous subcutaneous nodules made up of areolar connective tissue. In them nerve-fibers are frequently found.

Epulis is a fibrous growth originating from the gum, usually at the site of diseased teeth.

Myxoma is a benign tumor made up of mucous tissue. Is usually pale in color, round, lobulated, encapsulated, and feels semifluid. On section a thick, viscid fluid exudes.

Microscopically spindle and stellate cells with long processes that anastomose are seen. In the meshes between the cells and processes is the mucous material. This substance is precipitated by acetic acid.

They occur in sheaths of tendons and nerves and in nasal and pharyngeal polyps, and in combination with sarcoma. Mucoid growths forming from degeneration of fibromata are not true examples of myxomata.

Lipoma is a benign tumor made up of fatty tissue. Is yellow in color, round, lobulated, encapsulated, and soft. May be very large. Microscopically the cells resemble ordinary fatty tissue, except in being considerably larger and the connective tissue trabeculæ are also thicker than normal. Occurs most commonly in the subcutaneous tissue, in fasciæ, and in synovial membranes. Is slow in growth and will

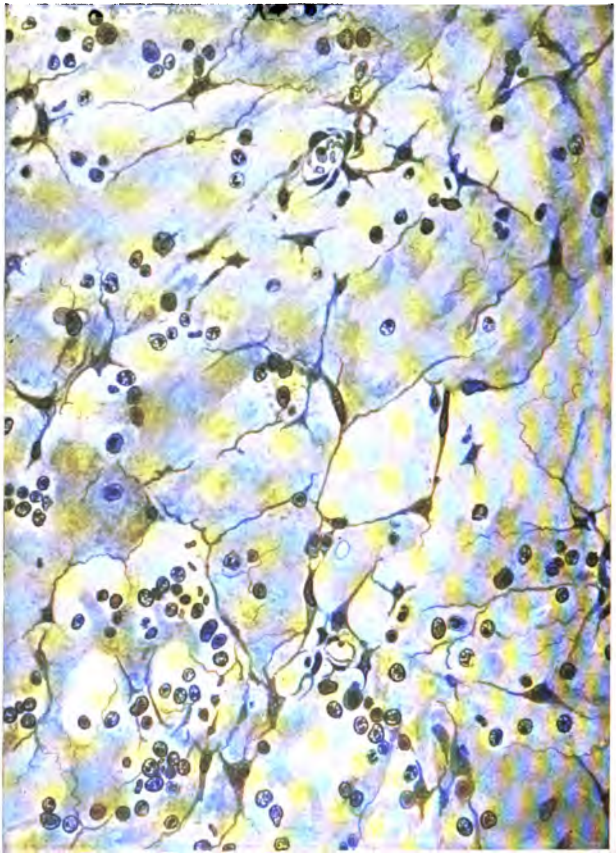


FIG. 33.—MYXOMATOUS FIBROMA OF THE NASAL MUCOUS MEMBRANE (Dürck)

Stellate connective-tissue cells joined together with protoplasmic processes; the intercellular substance has become myxomatous and contains abundant masses of leukocytes.

frequently persist even if the individual is much emaciated. Occurs in combination with sarcoma, myxoma, fibroma, and angioma.

Chondroma is a growth composed of either hyaline or fibrous cartilage.

Arises from periosteum or the medullary substance of the long bones. If it is found in localities where periosteum does not exist, as in testicles, is called an *enchondroma.*

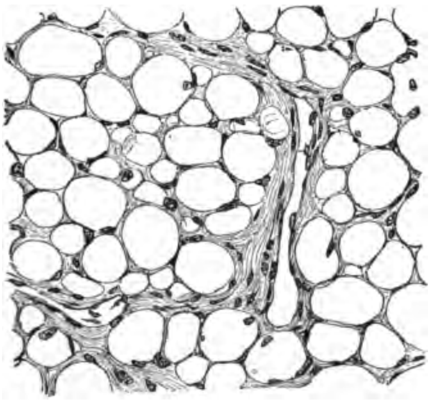


FIG. 34.—LIPOMA FROM THE REGION OF THE SHOULDER WITH RELATIVELY SMALL FAT CELLS. (M. Fl. Häm.) × 300 (Ziegler).

Is hard, encapsulated, and lobulated. Is slow in growth, may persist for years, and become very large.

Frequently undergoes mucoid degeneration and calcareous infiltration.

Is benign, but in combination with sarcoma may be quite malignant. Is also found in combination with lipoma, fibroma, and myxoma. An *ecchondroma* is a small overgrowth of cartilage. Are found on the edges of the articular, laryngeal, and nasal cartilages.

Osteoma is a tumor composed of bone. It may be a

result of inflammatory processes of the periosteum or be a distinct new growth.

If developing from a bone-forming tissue, is called a *homologous* osteoma.

If arising in a tissue that is not bone-forming, is called

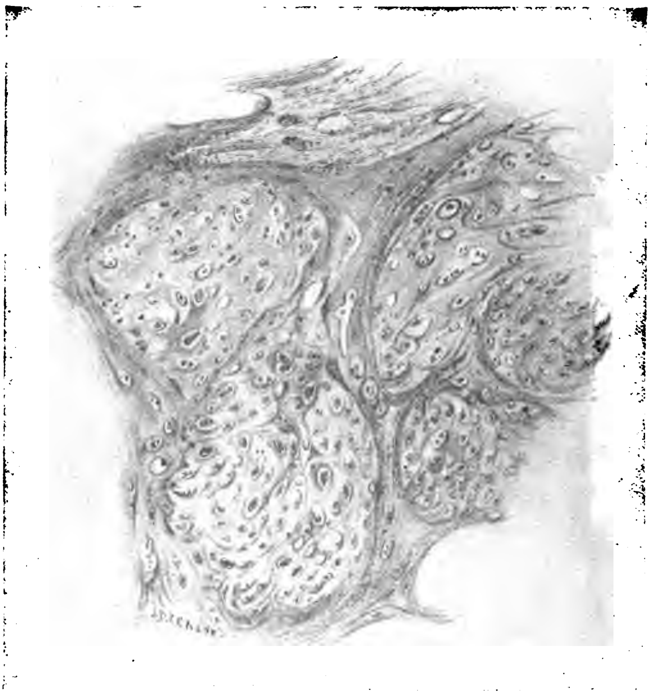


FIG. 35.—HYALINE CHONDROMA. Oc. 2; ob. 3 (McFarland).

a *heterologous* osteoma. The latter are found in the meninges, lung, and parotid gland.

An osteoma is a hard, bony, rounded, and more or less lobulated growth. Microscopically it presents quite typically the normal structure of bone. May be composed of spongy

or compact new bone, osteoma spongiosum and osteoma durum.

If the growth is small, circumscribed and flat, and arising from pre-existing bone, it is called an *osteophyte*. If irregular and projecting, an *exostosis*.

Occurs most commonly at the epiphyses of long bones. Is benign. May be in combination with cartilage, fibrous tissue, fat, or sarcoma, in which latter case it is malignant.

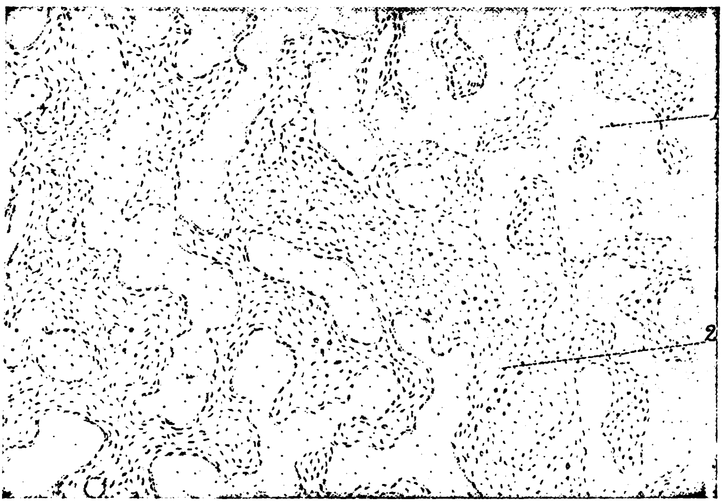


FIG. 36.—OSTEOMA OF THE LUNG. Hemat.; bleu de Lyon. × 75 (Dürck). 1, Bone-trabeculæ; 2, fibrous interspaces not presenting the characters of medullary spaces.

Myoma is a tumor composed of newly formed muscle-fibers. According as to whether the muscle is striped or voluntary, or unstriped and involuntary, we have the *rhabdomyoma* and the *leiomyoma*.

The first is very uncommon.

The latter occur frequently in the uterus and broad liga-

ment, but may arise wherever there is involuntary muscle. Are firm, round, lobulated growths, dark reddish in color.

Are benign, slow of growth, and frequently undergo cystic or calcareous degeneration. The cysts contain mucus.

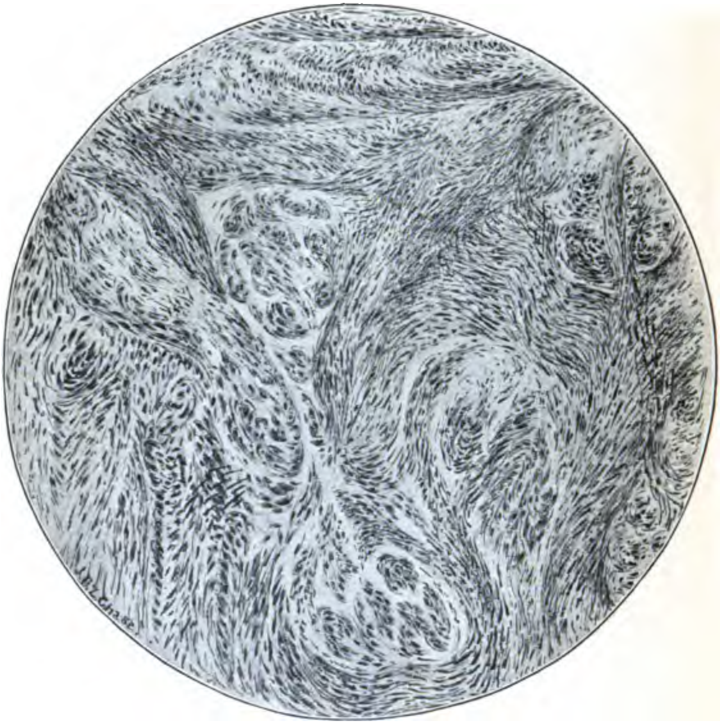


FIG. 37.—LEIOMYOMA OF THE UTERUS (UTERINE FIBROID). Oc. 4; ob. 3 (McFarland).

Usually are in combination with fibroma.

Neuroma is a tumor composed of nerve tissue. As the term has been applied to all growths found on nerves, two divisions are made, the *true* neuroma, which consists of

nerve tissue, and the *false* neuroma, which consists of fibro-connective tissue.

The true is called a *ganglionic* neuroma when ganglionic nerve-cells are present; if nerve-fibers only are present, is called a *fibrillar* neuroma.

Hemangioma is a tumor made up of blood-vessels.

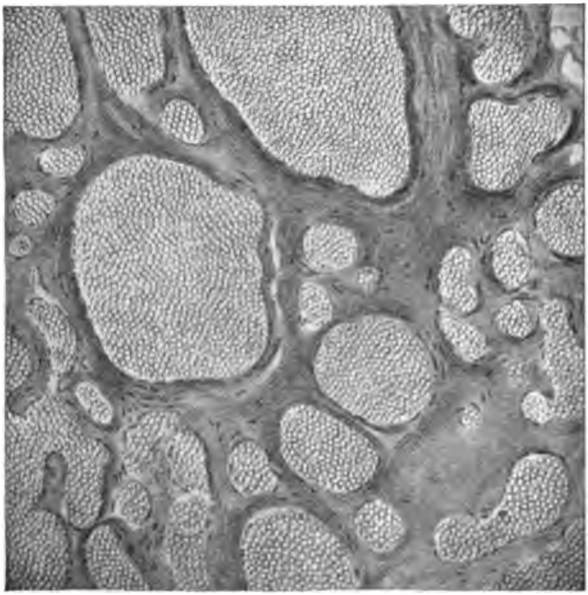


FIG. 38.—CAVERNOUS ANGIOMA (Warren).

Angioma simplex or nævus when the vessels are small and very much interwoven.

Cavernous angioma when the blood-spaces are large and separated by distinct fibrous bands. Resembles the structure of the corpus cavernosum of the penis.

Plexiform angioma when a group of more or less parallel blood-vessels become tortuous and widely dilated.

Lymphangioma is a tumor caused by a dilatation of

lymphatic vessels with an arrangement quite similar to that of the hemangioma.

An **odontoma** is a tumor resulting from the imperfect development of a tooth.

According to Sutton, there are the following varieties:

Those developing from:

The enamel organ	=	epithelial odontoma.
The tooth follicle	=	follicular odontoma. compound follicular odontoma. petrous odontoma. cementoma.
The papule	=	radicular odontoma.
The whole germ	=	composite odontoma.

1. *Epithelial odontoma* develop from the enamel organ. Microscopically they somewhat resemble an adenoma on account of the branching epithelial growths.

2. *Follicular odontoma* consist of a wall formed by an extended tooth follicle, the cavity of which is filled with a thick fluid and contains a part of an imperfectly developed tooth.

3. *Compound follicular odontoma* result from the sporadic ossification of a thickened capsule. They contain a number of small fragments of cementum or dentine or sometimes imperfectly formed teeth made up of cementum, enamel, and dentine.

4. *Fibrous odontoma* consist of the connective tissue capsule covering the tooth becoming so thick that the tooth is not able to be erupted.

5. *Cementoma* is a form of odontoma in which the thickened capsule over the tooth has undergone ossification.

6. *Radicular odontoma* forms after the crown of the tooth has been completed and while the roots are in the process of formation. It consists of dentine and cementum in varying proportions.

7. *Composite odontoma* refers to those hard tooth tumors which bear little or no resemblance in shape to teeth, but occur in the jaws, and consist of a disordered conglomeration of enamel, dentine, and cementum.

TUMORS OF EPITHELIAL TISSUES

A **papilloma** is a tumor composed of projections of fibrous connective tissue that are covered by one or more layers of epithelium, either squamous or columnar in type.

May be divided into the *hard* and the *soft* papillomata.

The *hard* occur on the skin as warts, also around the

FIG. 39.—TUFT OF PAPILLOMA OF THE BLADDER (Stengel).

genitalia as a result of constant irritation; in which situation are known as venereal warts. Are also found on the true vocal cords in the larynx. Are covered by squamous epithelium which commonly undergoes keratosis, a horny change. In this form the "pearly bodies" or "epithelial

pearls" are frequently found. These are made up of cells concentrically arranged, many of which have lost their nuclei and have become transformed into keratin. They are found only in squamous epithelium.

Papilloma covered by squamous epithelium are frequently found in the urinary bladder.

The *soft* papilloma occur in the intestine, and are covered by columnar epithelium. This form quite frequently undergoes malignant transformation.

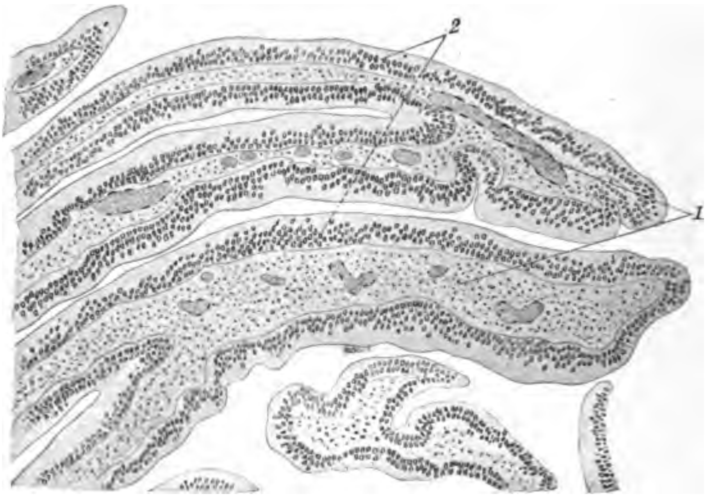


FIG. 40.—PAPILLARY ADENOMA FROM THE RECTUM. Hemat.-eosin. × 98 (Dürck).
1, Vascular stroma; 2, stratified cylindric epithelium.

The connective-tissue stalks may be simple projections or very complicated, branching outgrowths. They contain blood-vessels and lymphatics.

An **adenoma** is a tumor that in its structure resembles an epithelial gland. It is frequently very difficult to tell whether it is a true growth or only an enlargement of a normal gland.

In the new growth the tissues, though arranged typically, do not carry on any useful function. The secretion may be imperfect or there may be no duct through which it can escape.

Adenomata arise from epithelial glands, are circumscribed, encapsulated, and rounded, or nodular. Have been found in all glandular tissues.

Microscopically they consist of a framework of connective tissue, the meshes of which are covered by one or two

FIG. 41.—ALVEOLAR ADENOMA OF THE MAMMARY GLAND. Oc. 2; Ob. 9 (McFarland).

layers of epithelial cells that resemble in shape and size those of the normal glands. The important point that distinguishes these growths from malignant ones is the relation of the cells to the basement membrane. In the benign adenomata the membrane is preserved and the cells show no tendency to invade the surrounding tissue.

If the connective tissue and epithelium are in normal proportion the growth is called a *simple adenoma;* if the connective tissue predominates, a *fibro-adenoma.*

If the tumor has a pedicle, is known as an *adenomatous* polyp.

Through degenerations, particularly colloid or mucoid, an adenoma may become very large through cystic formation. Is then called an *adenocystoma.*

If villi extend into the acini in the above form the growth is called an *adcnocystoma papilliferum.*

FIG. 42.—FIBRO-ADENOMA OF THE MAMMARY GLAND (CANALICULAR FORM). Oc. 2; Ob. 3 (McFarland).

Hypernephromata are tumors that resemble the structure of the adrenal gland. They result from the growth of inclusions of aberrant adrenal tissue. Are found in the kidney, liver, broad ligament, and in other abdominal tissues.

Gliomata are growths composed of neuroglia or nervous connective tissue. As they arise from the epiblast they cannot be classified with the mesoblastic tumors.

Are usually small, reddish in color, and not distinctly limited from surrounding tissues.

Microscopically they are composed of cells with large nuclei and with long fine processes.

Blood-vessels may be numerous and many areas of hemorrhage present.

Are benign and slow-growing.

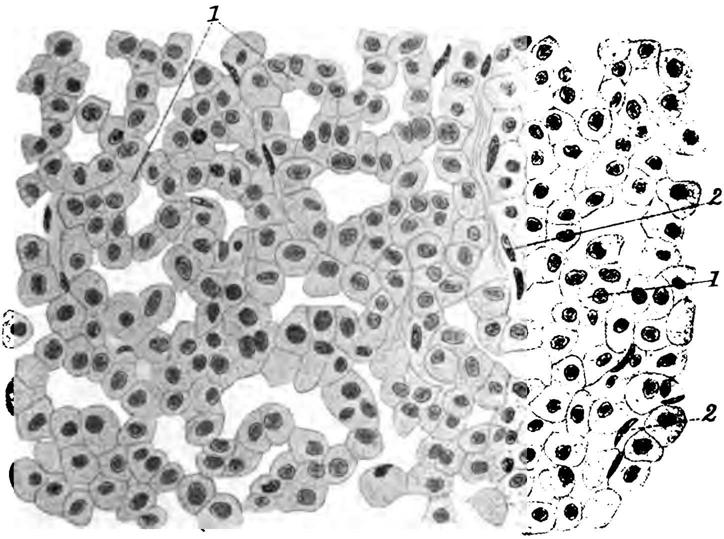


FIG. 43.—ADRENAL TUMOR FROM THE KIDNEY (HYPERNEPHROMA) (Dürck). (Hemat.-eosin.)

1, Large polygonal cells, containing an abundance of fat and arranged in tubes; 2, connective-tissue cells in the scanty stroma.

CARCINOMA

A **carcinoma** is a malignant tumor of epithelial origin. It is characterized by a marked proliferation of epithelium with infiltration into the surrounding tissues.

The epithelium is arranged atypically in a supporting framework made up of adult connective tissue.

The epithelial cells are not characteristic of the growth but they differ in some respects from the normal type. The diagnosis of carcinoma cannot be made from the cell, as there is no distinct cancer cell. The general arrangement of epithelium and connective tissue must be taken into consideration.

The carcinomatous epithelium frequently consists of cells

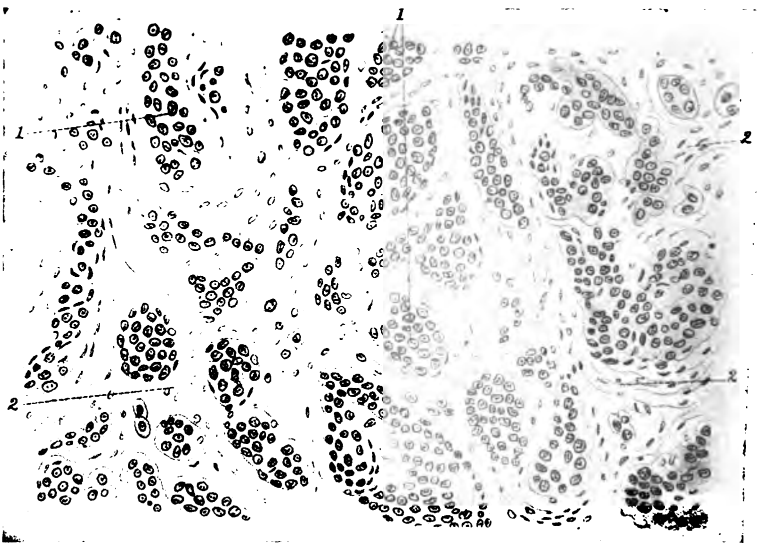


FIG. 44.—METASTATIC SIMPLE CARCINOMA OF THE DURA MATER. Hemat.-eosin. × 150 (Dürck).

1, Solid epithelial plugs lying within alveoli; 2, stroma.

many times larger than normal. Their nuclei may be unusually large, vesicular, and show a peculiar affinity for nuclear stains, a condition called *hyperchromatosis.*

They may divide by an atypical mitosis and give rise to peculiar arrangements of the chromatin. These cells multiply rapidly, and though at first round they may become almost any shape on account of the mutual pressure exerted.

In some cases giant cells occur. Tumors of this variety differ greatly in size, shape, color, and density.

Carcinomata are composed of two types of tissue, epithelial and connective, cells and stroma. According to the one that predominates, carcinomata are called *medullary* when the cells are more numerous; *scirrhus* when the tumor is rich in connective tissue.

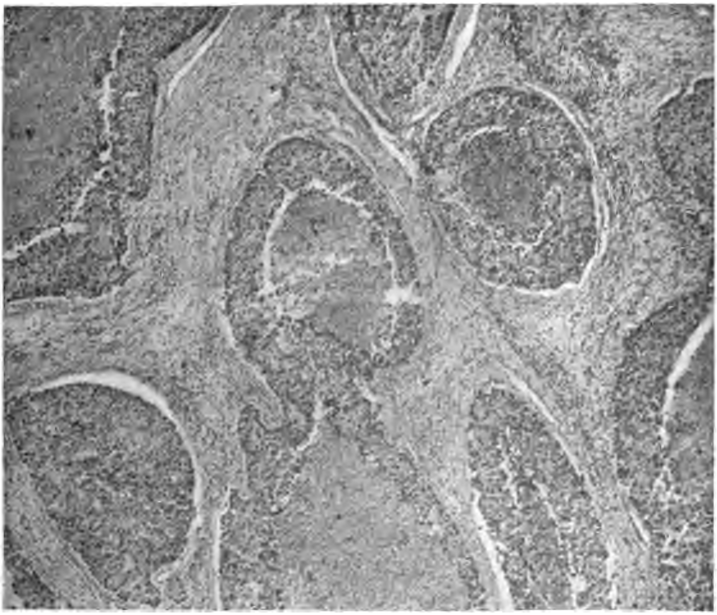


FIG. 45.—MEDULLARY CARCINOMA OF THE BREAST, SHOWING NECROSIS IN THE CENTER OF THE COLUMNS (LOW POWER) (Warren).

The first is soft, the second hard.

Well-developed blood-vessels and lymphatics are found in the stroma, which is most likely derived chiefly from preexisting connective tissue, but a certain amount is probably new-formed. Elastic fibers are present in the infiltrating

portion of the growth. The cellular elements originate from the epithelium normal to the part involved and frequently retain the characteristics of the primary cell.

The more closely connected it is with the original cell, the more does the carcinoma cell resemble it. The further away it is, the greater is the variation. There is then a tendency to revert to the round undifferentiated embryonal type. Between the cells no fibrillary substance is found.

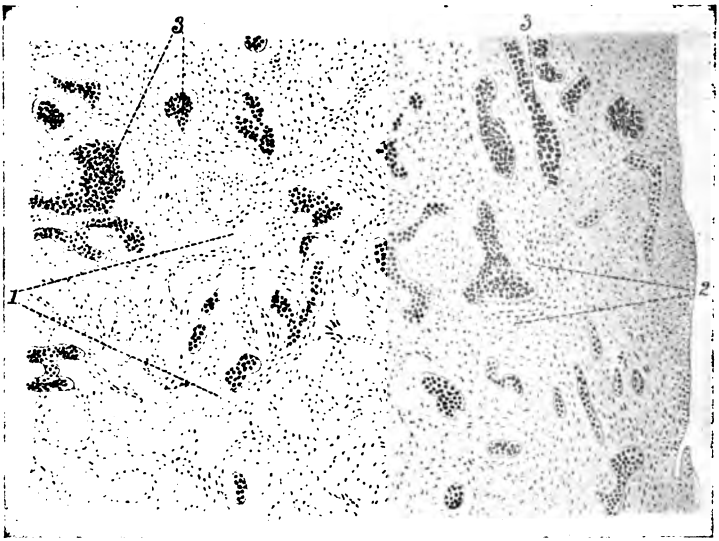


FIG. 46.—SCIRRHUS CARCINOMA OF THE MAMMARY GLAND. Hemat.-eosin. × 50 (Dürck).

1, Broad masses of fibrous connective tissue; 2, more cellular masses of connective tissue; 3, narrow cancer-alveoli.

In the carcinoma the cells frequently undergo degeneration, and usually of a form peculiar to the parent tissue. If it arose from squamous epithelium keratin is found; colloid or mucoid material if derived from mucous membranes. The tumor may break down and undergo a fatty change, most common in the mammary gland.

A carcinoma may become infected and show marked inflammatory changes which may be so great as to somewhat disguise the true character of the growth. There will be an infiltration of the tissues with leukocytes.

Microscopically a carcinoma consists of columns of cells running in all directions, separated from one another by fibrous tissues. These columns give the appearance of alveoli filled with epithelium. The columns are branched into numerous subdivisions, giving a complicated root-like structure.

As the tumor grows these cells infiltrate and ramify in all directions, occupying usually the lymphatic spaces.

As there is no intercellular substance the cells easily break away from the main mass and are carried to the neighboring lymph-nodes. This may take place very early and give rise to extensive metastasis. These secondary growths are usually similar in character to the primary.

A **squamous epithelioma** is a carcinoma that has arisen from a surface covered by stratified epithelium such as skin and certain mucous membranes. It occurs most commonly on the cervix, the skin of the face, penis, vagina, and esophagus, especially wherever there is a junction of skin and mucous surfaces.

It makes its appearance as an indurated mass in which ulceration takes place rapidly and exposes a circular surface with raised, hard edges. Sometimes it looks at first like a small wart.

Columns of these cells penetrate the tissues and on account of pressure arrange themselves in successive layers, the inner ones being almost flat and cornified, forming the *epithelial pearls*. *Hyperkeratosis* is the term used to indicate the cornification.

The presence of these pearls does not indicate that the tumor is necessarily malignant; they mean that the growth was derived from squamous epithelium. They are also not always found in squamous epitheliomata. The growth may have been so rapid as not to have allowed cornification to take place.

The cells are usually quite large and may show numerous "prickles."

This form of carcinoma differs greatly in its malignancy. Some may exist for several years without showing much tendency to spread, but may suddenly grow and cause extensive destruction of tissue with subsequent death of the patient.

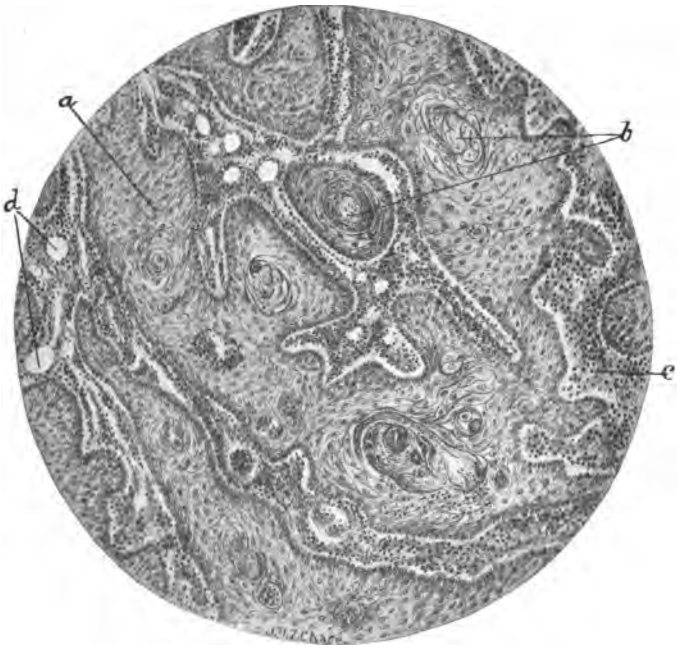


FIG. 47.—SQUAMOUS EPITHELIOMA (McFarland).
a, Epithelial masses; *b*, epithelial pearls; *c*, connective tissue; *d*, capillary blood-vessels.

A *rodent ulcer* in its microscopic appearance resembles a variety of squamous epithelioma, but has peculiar clinical manifestations.

For many years, eight to twelve, there may be present a

smooth rounded nodule about the size of a pea. Is a solid growth originating beneath the epidermis, and composed of sebaceous gland ducts filled with epithelium.

For apparently no reason it may ulcerate and the most extreme destruction of all neighboring tissues take place.

It arises generally on the face of people over fifty years of age. It does not infect lymph-glands, nor give metastasis. As a rule, is solitary, but may be multiple and may extend in duration over many years.

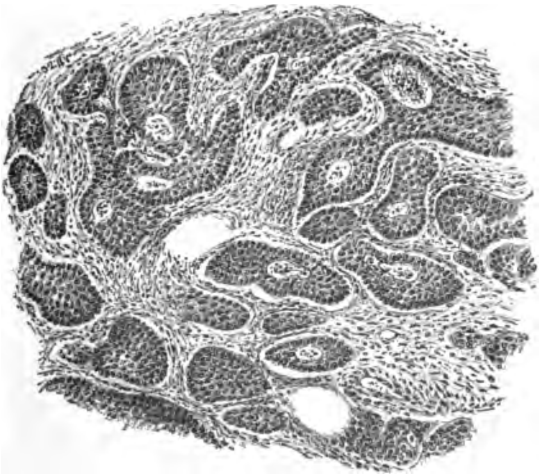


FIG. 48.—GLANDULAR CANCER OF THE CERVIX UTERI (Stengel).

An **adenocarcinoma** is a cancer in which the glandular structure is to a great extent preserved, but the epithelium has taken on a proliferative growth. It either breaks through the basement membrane or else fills up the acini with numerous layers of cells. Are commonly found in the stomach, intestine, and uterus. Grow rapidly, give metastasis, and quickly prove fatal.

The development of carcinoma differs greatly in different people. In some cases a continued mild irritation may precede. The growth may be very slow, but if for some reason

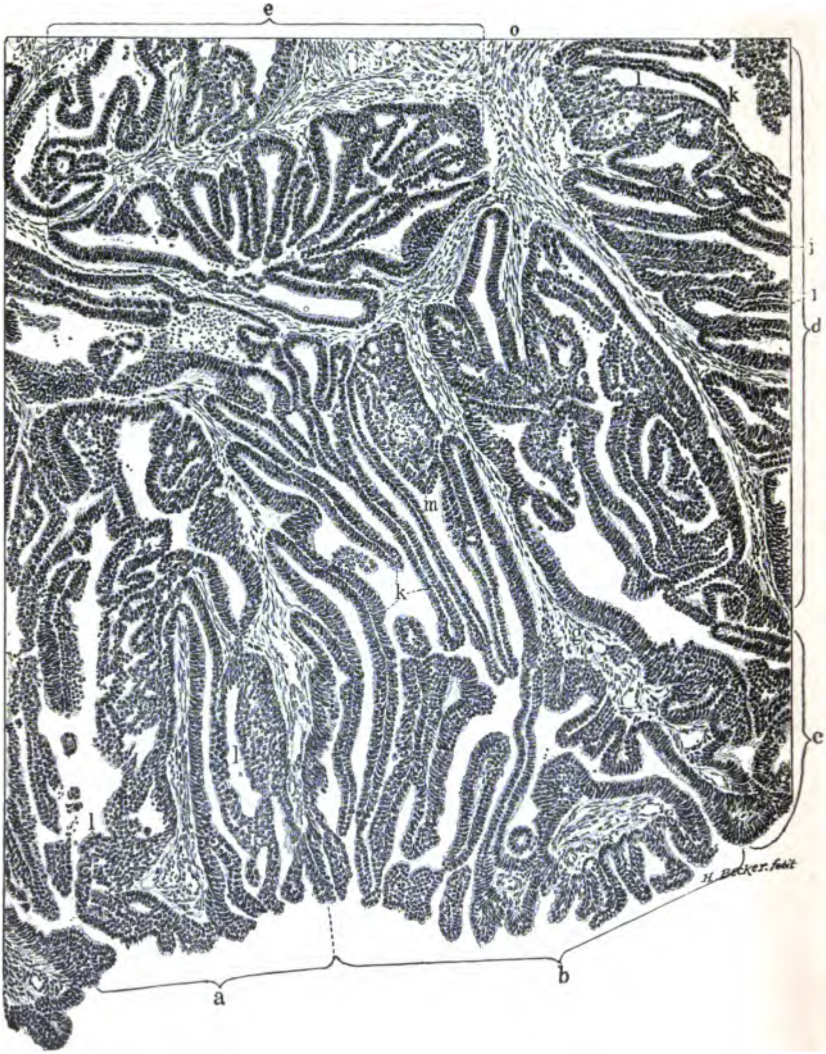


FIG. 49.

there is an increase in the nutrition, as in the pregnant uterus, it may suddenly become rapid.

If the growth is rapid and metastasis extensive the health of the patient suffers and cachexia develops. This may be the result of pain, of suppurative conditions or from the absorption of toxic substances resulting from the disturbance of metabolism.

The etiology of carcinoma is still obscure. Heredity is apparently clear in many cases as a predisposing cause.

Age is of importance, the majority of cases appearing after the age of thirty-five, a time when the resisting power of the tissues is beginning to diminish.

Carcinoma is more common in women than in men. In women it is in the genital organs, in men in the intestinal tract.

Irritation and injury seem to at least be of some importance as exciting causes, although in themselves it is doubtful if they can give rise to a carcinoma.

Loss of resistance of the connective-tissue stroma has been advanced, but does not seem logical. Many observers have tried to prove that these growths are infectious processes, the results of parasitic activity. Many cellular inclusions resembling protozoa have been found, but the general opinion at present is that these bodies are nothing more than degenerated cells, or secretions of cells. Experiments to prove the infectious nature of carcinomata have not been generally successful. The transplantation of cancer tissue into a normal individual has failed. But when placed in another situation in the person from whom the tissue was excised growth

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FIG. 49.—ADENOCARCINOMA OF THE BODY OF THE UTERUS. (Cullen). *o*, May be likened to a main stem from which arise numerous secondary stems, which in turn give off delicate terminals, consisting entirely of epithelial cells. The glands may be divided into groups *a*, *b*, *c*, *d*, and *e*, by the stems of stroma *f*, *g*, and *h*. The stems are covered by several layers of cylindric epithelium, while projecting into the gland cavities are long slender ingrowths of epithelium, devoid of stroma, as seen in *i*. Very delicate ingrowths consisting merely of two layers of epithelium are seen at *k* and *k*. At *l* the epithelium is several layers in thickness, and at *m* many layers with leukocytes. The arborescent character of the growth and peculiar gland grouping are characteristic of adenocarcinoma.

has followed. This has frequently been considered proof of the parasitic nature. It probably means nothing more than that the pieces of tissue have found surroundings favoring their growth; a condition such as occurs in skin-grafting.

Bacteria, protozoa, sporozoa, gregarinæ, blastomycetes, amebæ, and fungi have all been suggested as the cause. These claims, however, rest upon the form of the bodies and

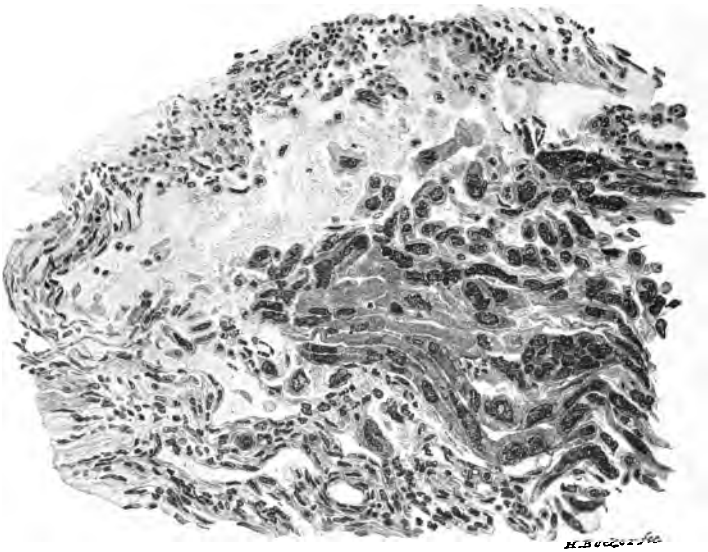


FIG. 50.—SYNCYTIAL MASSES INVADING A VENOUS CHANNEL IN A CASE OF DECIDUOMA MALIGNUM (J. Whitridge Williams).

their staining properties, not upon cultivation and inoculation. Until these latter can be carried out the parasite theory must remain unproven.

SYNCYTIOMA

A *syncytioma* or *deciduoma malignum* is a tumor that develops within the uterus from the chorionic villi. It is included by many under the sarcomata on account of its close

resemblance to that class of tumor. It probably belongs to the organoid or epithelial group of tumors. Is frequently referred to as a *chorioepithelioma.*

The chief cells of the tumor originate from the syncytium. These cells invade the blood-sinuses and the uterine muscle, causing extensive and rapid destruction. Myxomatous degeneration and necrosis are common.

The growth gives early metastases, particularly to lung and vagina, is nearly always very rich in blood, and quickly proves fatal.

Microscopically various cells are seen. Very large ones containing many large nuclei, rich in chromatin, are formed by direct division.

Others much smaller with single well-formed nuclei and containing glycogen. Some that resemble lymphocytes, and all kinds of forms resembling the above types more or less closely.

These tumors frequently succeed a hydatid mole or may follow a normal or interrupted pregnancy.

TERATOID TUMORS

A **dermoid cyst** is a tumor that belongs to the teratoid class. That is, it is one in which the three primary embryonic layers are represented. On account of the skin and its appendages, such as sebaceous glands, hair, and teeth, being the most conspicuous elements, the cyst is spoken of as a dermoid.

They are the result of disturbances of development and of the inclusion of the embryonic layers. Are most common in the ovary and in the orbit. They occur frequently in those parts of the body where fetal clefts have united, in the median fissures of the body, at the branchial clefts, etc. They are, however, found, as in the ovary and testicle, where the origin must be different. According to Wilms, they here are the result of parthenogenesis.

A **teratoma** is a tumor similar to the dermoid in that it has representatives of the three embryonic layers. The term is restricted, though, to those in which certain portions

are more completely developed. There may be a rudimentary limb or gland. It is to this group that the double monsters belong.

Teratomata are usually found either at the anterior or posterior ends of the vertebral column, along the lines of the median fissures.

CYSTS

A *cyst* is a circumscribed collection of fluid. Most of the cystic cavities are lined either by epithelium or endothelium.

The contained material may be semifluid, serous, mucous, or purulent if infection has occurred.

Cysts may be either single or multilocular if divided into numerous compartments by fibrous partitions. These trabeculæ may break down and convert a multilocular into a simple cyst.

Cysts may be divided into the following:

1. *Retention* cysts resulting from an obstruction to the outflow of the secretion of a gland.
2. *Exudation* cysts, those formed by an increase of fluid in a closed cavity, as in the tunica vaginalis.
3. *Liquefaction* cysts result from the breaking down of the central portion of solid tumors.
4. *Parasitic* cysts may occur on account of an inflammatory reaction around the parasite, or may be formed directly by it, in its development.
5. *Dermoid* cysts belong to the teratomata, where they are described.

CHAPTER X

INFECTION AND IMMUNITY

By **infection** is meant the successful invasion of the tissues by an organism. The mere presence of the bacterium within the body is not sufficient to cause infection; it must enter the tissues and give rise to symptoms that indicate a diseased condition.

There are normally many organisms contained within the body, particularly in the alimentary canal, but they give rise to no pathologic conditions until they leave their accustomed habitat.

Infection therefore means the entrance of organisms into the body with subsequent injury to the tissues involved.

By an infective disease is meant one that is the result of the entrance into and the multiplication of the organisms within the body.

The symptoms in such a condition are the result of toxins produced and not of mechanical disturbances. As a rule, no symptoms appear immediately after the entrance of the bacterium into the body, as there is not sufficient toxin present. The time between the inoculation and the appearance of the symptoms resulting from the toxins is known as the *period of incubation.* This differs greatly in different diseases.

Infection may be affected by certain peculiarities of the infecting organisms and of the infected individual.

The virulence or the disease-producing capacity of the micro-organisms may vary. An organism may occur in combination with some other bacterium which may be beneficial or detrimental. The number of the organisms and also the avenue of entrance affect the severity of the infection.

The infections may be *exogenous,* those entirely foreign

to the body, or *endogenous*, those arising from organisms already within or upon the body. These latter gain entrance into the tissues through the skin and mucous membranes, the respiratory tract, the digestive apparatus, the sexual organs, and the external ear.

To have infection taking place virulent organisms must enter the body in sufficient numbers, and they must find a soil suitable for their growth.

When two organisms invade the body at the same time, the condition is known as *mixed infection*.

If after one organism has caused tissue changes another gains entrance and gives rise to pathologic conditions, it is called a *secondary infection*.

By **immunity** is meant the power to resist disease. An individual may be exposed to infection, but on account of some ability to resist does not acquire the disease.

By *susceptibility* is meant the lack of resisting power.

Immunity is either *natural* or *acquired*.

The natural form is an inherited resisting power that is common to certain races of men or animals.

The acquired is that form which has been obtained after birth, and may be either active or passive.

Immunity is termed *active* when it results from the action of the cells within the body either in destroying the bacteria or in injuring them.

Is called *passive* when it results from the introduction of foreign substances into the blood.

Active immunity is that which follows an attack of an infectious disease, and may last for a varying period. It may be very brief, as in cholera; for a longer time, as in typhoid; or sometimes for life, as in smallpox. It may result from the inoculation of a weakened virus, as in vaccination, or it may follow the introduction into the body of bacterial toxins without the micro-organisms.

Passive immunity is that which is obtained by the introduction of the serum from an immunized animal into the blood of a non-immune individual. It is supposed that in the serum of the former there is a substance, spoken of as

antitoxin, that neutralizes the toxin in the blood of the infected animal.

By immunity is implied that not only the bacteria are destroyed but that their toxic effects are neutralized as well.

It must also be remembered that immunity is a comparatively relative term. The degree of immunity may be reduced by unhygienic surroundings, by noxious gases, by fatigue, exposure to abnormal temperatures, abnormalities of diet, effect of drugs, pre-existing disease and by injuries.

THEORIES OF ACQUIRED IMMUNITY

1. That the bacteria growing in the body used up some material that was necessary for their growth and after dying left a soil unsuitable (Pasteur and Klebs).

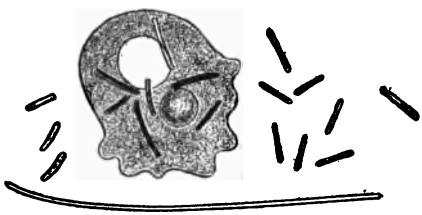


FIG. 51.—LEUKOCYTE WITH INCORPORATED BACILLI, ILLUSTRATING PHAGOCYTOSIS (Metchnikoff).

2. That in the growth of the bacteria there were elaborated substances that inhibited their future development or activity (Wernich and Chaveau).

3. That the cells which have successfully defended the body against the action of the bacteria acquire and retain a greater power of resistance.

4. That it is due to the activity of certain cells, called phagocytes. This is supposed to depend upon the power certain cells have of ameboid motion, by means of which they are able to surround and take up bacteria and destroy them.

Metchnikoff believes that immunity is the result of the

positive and negative chemotaxis existing between the phagocytic cells and micro-organisms. He divides the cells into:

(1) Microphages: eosinophiles and neutrophiles.

(2) Macrophages: large lymphocytes, endothelial and connective-tissue cells.

When the bacteria gain entrance into the body the phagocytes are attracted to that portion and they attempt to ingest and destroy the invaders. If the immunity of the animal is high, many of the organisms will be found within the cells; if the immunity is slight, few cells will contain bacteria.

5. That the blood itself contains substances that exert a destroying influence upon the micro-organisms or its products. The proteid occurring in animals naturally immune is called a *sozin;* if in acquired immunity, a *phylaxin.* If these bodies destroy the bacteria, they are known as *mycosozins* and *mycophylaxins;* if they neutralize the toxins, they are known as *toxosozins* and *toxophylaxins.*

The sozins act upon the blood-cells and bacteria, causing cytolysis or bacteriolysis, but are themselves destroyed by heating at a temperature of 55° to 60°C. for an hour. These bodies are also known as *alexins.*

The phylaxins are the true antitoxic bodies. They are more resistant to heat, are capable of acting after being exposed to a temperature of 80° C.

6. Ehrlich's Lateral-Chain Theory. This receives its name from its analogy to the benzole ring, but is indicated in terms that can be applied to hypothetic morphologic bodies.

In this it is claimed that immunity depends upon the presence or absence of "receptors." The receptor is that body attached to the cell by means of which the cell is acted upon by various substances, nutritive or otherwise. Each receptor is supposed to be so formed as to unite with other bodies of a definite character. In the action of the organisms upon the cells the toxic substances are considered as being formed of two bodies, the "haptophorous" and the "toxophorous" groups. The combination is supposed to take place as follows: The haptophoric group unites with a certain definite receptor, and by so doing interferes with the normal

function of the cell. The toxophoric group then is able to act directly upon the cell. If it is very powerful the cell is destroyed, and if a sufficient number are involved the individual may die.

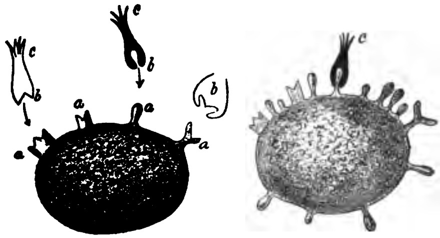
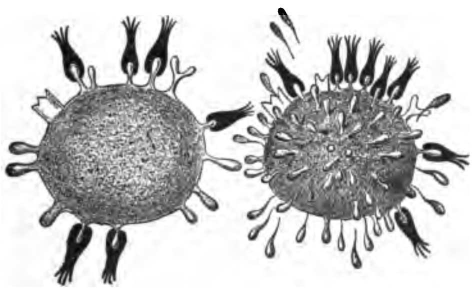


FIG. 52.

Cells with various receptors or haptophorous groups of the first order (*a*), adapted to combination with the haptophorous groups (*b*) of various chemical compounds brought to them. It will be noted that there is no mechanism by which the toxophorous elements of the molecules (*c*) can be brought to the cell.



FIGS. 53 AND 54.—SHOW THE REGENERATION OF THE CELL-HAPTOPHORES OR RECEPTORS TO COMPENSATE FOR THE LOSS OF THOSE THROWN OUT OF SERVICE.

If this does not occur, the cell will be so stimulated that new receptors similar to the ones destroyed will be formed. There may be such a fresh supply that many will be cast forth into the circulation. These cast-off receptors form

the antitoxin, and by coming in contact with the poison unite with and neutralize it.

In bacteriolysis and hemolysis the destruction is brought about indirectly. Besides the cells, two other bodies are concerned. One is known as the *amboceptor*, *intermediate* or *immune body*. It is found during the production of the cytolytic sera, is not destroyed by heat up to 80°C., and is consequently termed thermo-stabile.

The second body, known as the *complement* or *alexin*, is

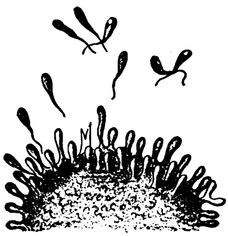


FIG. 55.—SHOWS THE NUMBER OF HAPTOPHORES REGENERATED BY THE CELL BECOMING EXCESSIVE, THEY ARE THROWN OFF INTO THE TISSUE JUICE.

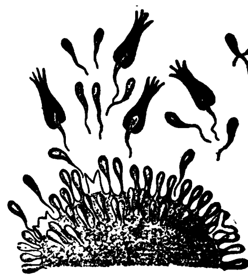


FIG. 56.—EXPLAINS WHAT ANTITOXINS ARE AND HOW THEY ARE FORMED.

The liberated receptors in the tissue juice and in the blood, possess identical combining affinities with those upon the cell, and meeting the adapted haptophorous elements in the blood, combine with them, thus keeping them from the cells.

normally present in the serum, is destroyed by a temperature of 55° C., and is termed thermo-labile.

In this the complement unites with the amboceptor, which in turn joins with the receptor, in this way allowing the destructive effect to take place upon the cell.

In acquired immunity the cells of the invaded animal form large amounts of the amboceptor, which, being free within the blood, unites with and neutralizes the toxins. If the supply is sufficient, the individual will recover. In passive

acquired immunity large numbers of the amboceptors are directly introduced into the patient, and in this way effect a cure.

If an animal, as a rabbit, is injected with the serum of another animal, as a dog, it will be found that after giving several doses, each a few days apart, the serum of animal I will precipitate the serum of animal II when placed in a test-tube. This occurs even in very high dilution.

If instead of the serum the erythrocytes are used, it will be found that the serum from No. I will dissolve the red cells of No. II.

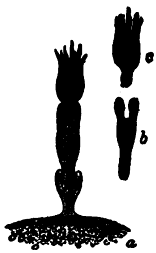


FIG. 57.—COMBINATION OF CELL (*a*), AMBOCEPTOR (*b*), AND COMPLEMENT (*c*).

The amboceptor may unite with the cell, but cannot affect it alone. The complement cannot unite with the cell except through the amboceptor, having no adaptation to the cell directly.

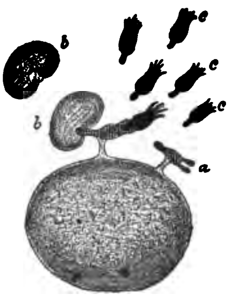


FIG. 58.

Cell with receptors of the second order (*a*) by which the cells fix useful molecules, of albumins, etc., on one hand (*b*), and zymogen molecules (*c*) on the other hand, and make use of the one substance through the action of the other.

The substance causing the first reaction is called a *precipitin;* that in the second case a *hemolysin.*

By using various cells certain substances acting upon specific structures will be obtained; these are known as *anti-bodies.*

These anti-bodies receive special names according to their method of action upon the cells.

Those that dissolve cells being known as *cytolysins;* if

they neutralize ferments, as *anti-enzymes;* if they cause agglutination, as *agglutinins.*

The substances destroying the cells receive various names according to the specific cells acted upon, the destruction being known as *lysis.*

Thus a *bacteriolysin* causes *bacteriolysis;* a *spermatolysin, spermatolysis.*

The bacterial poisons are divided into three classes according to their strength, all of which, however, have the one point in common that they contain haptophore elements. They are known as *toxins, toxoids,* and *toxones.*

CHAPTER XI

VEGETABLE PARASITES

Under the heading of **Fungi** belong the mildews, yeasts, and bacteria. They are plants of very low organization, do not contain chlorophyl, except very rarely, and derive their nutrition from organic compounds.

This class includes the:

Basidiomycetes.
Mycomycetes, the common moulds.
Phycomycetes, the mucor moulds.
Blastomycetes or *Saccharomycetes*, yeast fungi.
Schizomycetes, the bacteria.

They may all be parasitic upon and within the body of man, animals, and other plants. The bacteria are especially important on account of their relation to disease and their bearing upon general hygiene and preventive medicine.

They break up the complex organic compounds into simpler ones, and if they derive their nutrition from dead substances are called *saprophytes;* if from living tissues, *parasites;* both are found in man.

The moulds occur as threads or hyphæ, in a tangled mass, the mycelium, from which filaments covered with spores arise.

The **Basidiomycetes** have spores borne upon basidia.

The *Achorion schoenlenii* is the fungus of *favus* or *tinea favosa.* It is found to consist of a mycelium of non-segmented hyphæ from which there extend at right angles numerous branches. The hyphæ show lateral buds and the "yellow bodies" of Kral. The mycelia divide into oval bodies or spores. The free ends only seem to be capable of reproduction, and peculiar bodies, called *conidia*, develop upon them. This parasite is usually found upon the head;

it develops within the hair-follicle, surrounds the bulb, and penetrates different layers of the hair.

The lesions are yellowish round plates, varying in size from a pinhead to a dime, have a saucer-like appearance, and are covered by crusts through which hairs pass. The crusts are made up of masses of hyphæ and conidia, are easily lifted, and leave a depressed ulcer which contains a drop of thick yellow fluid.

If the crusts are not removed they may unite to form large masses. The hairs are lusterless and easily plucked out.

The fungus is transmitted from one person to another and may be found in parts of the body where no hair is present, as in the nails.

Mycomycetes.—The mycelia contain many cells. The following are the more important of this group:

The *oidium albicans*, which is the cause of *thrush*.

Its microscopic appearance varies greatly. Usually from the yeast-like cells there develop long cylindric hyphæ, consisting of united elongated cells from which numerous oval sprouts are given off at the junctions. Bulbous swellings are often found on the ends of the mycelia.

Is most commonly found in the mouth on the tongue, but has been observed in the esophagus, intestines, and vulva. It appears as milk-white patches surrounded by hyperemic zones.

Is probably saprophytic, as a rule, and is able to obtain lodgment in living tissues only when the vitality of the individual is much lowered.

The *trichophyton tonsurans*, the parasite of "barber's itch," consists of mycelia divided into hyphæ and forming many conidia.

Is commonly saprophytic, but when parasitic it grows usually on hairy parts and penetrates the shaft of the hairs, causing them to become brittle. If upon the head there results rounded, scaly, and red bald areas varying in size, from which short hairs project.

If the skin is free from hairs the disease appears in red

patches with a vesicular or scaly surface. These areas may extend from one portion to another, the patch first involved healing as others are affected.

The organism multiplies between the horny and cellular layers of the epidermis. Sometimes it is found about the finger-nails, causing them to become cloudy, scaly, and brittle, with inflamed roots.

A parasite supposed to be the same as this is found in sycosis parasitica and eczema marginatum. Ringworm also results when this fungus is inoculated upon the skin.

The dusty material present is composed of dried epithelium and fungus spores, the latter often being arranged in chains.

The *microsporon furfur* is the fungus causing *pityriasis versicolor.* It is composed of delicate threads with rather small conidia, which may be empty or contain spores. Between the threads are found spherical groups of spores.

Upon the skin it forms peculiar pale brownish or yellowish areas, more or less circumscribed, and varying in size from pin-points to spots several centimeters wide.

The *microsporon minutissimum* causes *erythrasma.* The mycelia consist of bifurcating threads which may contain minute spores.

It occurs on the skin of the axilla, inguinal and natal folds as small, rounded, or irregular well-defined patches of a reddish or brownish color.

Several species of the *Aspergillus* are known to be pathogenic to man, the *A. flavus*, *A. fumigatus*, and *A. niger.*

The most severe results follow when this fungus develops in the internal organs of the body, particularly in the lung. It occurs in man only when the resistance of the lungs is already much lowered by tuberculosis or some other preexisting disease.

The **Phycomycetes** are destitute of chlorophyl; the mycelia are unicellular at first, but sometimes become septate. Reproduce usually by spores.

To this class belong the *mucor* moulds, two of which have been found in man as the cause of disease. May give rise

to inflammation of the external ear and have been found in the internal organs.

The **Blastomycetes,** or saccharomycetes or yeasts, are frequently found in man as harmless saprophytes; are constant in the alimentary canal, especially in the mouth and stomach. If they gain entrance into the bladder and come in contact with a urine containing dextrose, fermentation with gas-formation may take place.

They occur as microscopic, spherical or ovoid, chlorophyl-free, unicellular vegetable organisms. They reproduce by the formation of buds, which after attaining some size, break off and carry on an independent existence. Sometimes in old cultures when the nutritive material is scanty the yeast cells develop into long cylindric hyphæ that do not bud.

The many peculiar bodies found in cancer, such as Russell's fuchsin body, Plummer's bodies, etc., are believed by many to be blastomycetes, but there is little evidence to support such a view.

The **Schizomycetes** or bacteria constitute the most important group of parasites.

The best method of grouping them is that of Migula, part of which is as follows:

I. Family Coccaceæ.—Cells globular, becoming slightly elongate before division, which takes place in one, two, or three directions of space. Formation of endospores rare.

1. *Streptococcus.*—Division in one direction of space only, producing chains of organisms like strings of beads. No flagella.

2. *Micrococcus.*—Division in two directions of space, so that fours or tetrads are often formed. No flagella.

3. *Sarcina.*—Division in all three directions of space, leading to the formation of bale-like packages of cocci. No flagella.

4. *Planococcus.*—Division in two directions of space like micrococci. Flagellated.

5. *Planosarcina.*—Division in three directions of space like sarcina, but have flagella.

II. Family Bacteriaceæ.—Cells more or less elongate,

cylindric, and straight. Never form spiral windings. Division in one direction only, transverse to the long axis.

1. *Bacterium.*—Without flagella. Occasional endospores.

2. *Bacillus.*—Flagella arising from all parts of the surface. Endosporulation usual.

3. *Pseudomonas.*—Flagella attached only at the end of the cells. Endospores rare.

III. Family Spirillaceæ.—Cells spirally twisted like a corkscrew, or short and curved and representing segments of the spiral. Division only transverse to the long axis.

1. *Spirosoma.*—Rigid. Without flagella.

2. *Microspira.*—Rigid. Have one, two, or three undulating flagella at the ends.

3. *Spirillum.*—Rigid. Having from five to twenty curved or undulating flagella at the end.

4. *Spirochæta.*—Serpentine and flexible. Flagella not observed. Probably swim by means of an undulating membrane.

IV. Family Mycobacteriaceæ, to which belongs the:

1. *Actinomyces.*—Cells in their ordinary form appearing as long branched filaments; growth coherent, dry or crumpled. Produce gonidia-like bodies. Cultures generally have a moldy appearance due to the development of aerial hyphæ. Have no flagella.

V. Family Chlamydobacteriaceæ, to which belong:

1. *Cladothrix.*—Characterized by pseudo-dichotomous branchings. Division transverse. Multiply by the separation of entire branches.

2. *Crenothrix.*—Cells united to form unbranched threads, which in beginning divide transversely. Later divide in all three directions.

3. *Phragmidiothrix.*—Cells at first united into unbranched threads. Divide in three spaces.

4. *Thiothrix.*—Unbranched cells enclosed in a delicate sheath. Divide in one direction. Contain sulphur granules.

VI. Family Beggiatoaceæ.—Cells united to form threads which are not surrounded by an inclosing sheath. Septa scarcely visible. Division transverse. Motile.

1. *Beggiatoa*.—Cells contain sulphur granules.

A more common but less accurate method of classification divides bacteria into:

1. *Bacillus*.—A rod-shaped organism that is not curved or twisted upon itself. Having one diameter distinctly greater than the other.

2. *Coccus*.—Any small spherical organism:

(*a*) *Diplococcus* when occurring in twos.

(*b*) *Streptococcus*, if in chains.

(*c*) *Staphylococcus*, when in bunches like grapes.

(*d*) *Tetracocci*, when division is in two directions and the individuals remain attached.

(*e*) *Sarcina* when dividing in three directions, giving rise to bale-like packages.

(*f*) *Zoöglea* when in irregular masses.

3. (*a*) *Spirillum*.—An organism twisted like a corkscrew and rigid; usually has polar flagella.

(*b*) *Spirochæta*, when cell is flexible, long, slender, and without flagella.

(*c*) *Vibrio*.—Short, bent like a comma, usually with a single end-flagellum.

According to the presence or absence of the flagella bacteria are divided into:

I. *Gymnobacteria*, forms without flagella.

II. *Trichobacteria*, forms with flagella.

1. *Monotricha*.—A single flagellum at one end.

2. *Lophotricha*.—A bundle of flagella at one end.

3. *Amphitricha*.—A flagellum at each end.

4. *Peritricha*.—Flagella arising from all parts of the surface of the organism.

Bacteria are composed of plasma or microprotein surrounded by a cell membrane; they sometimes possess a capsule.

Most cocci are non-motile; the other varieties may possess flagella and in that way be able to propel themselves.

Multiplication takes place by simple fission or splitting into two. Occurs very rapidly if there is enough nutritive media present and the surrounding conditions are favorable.

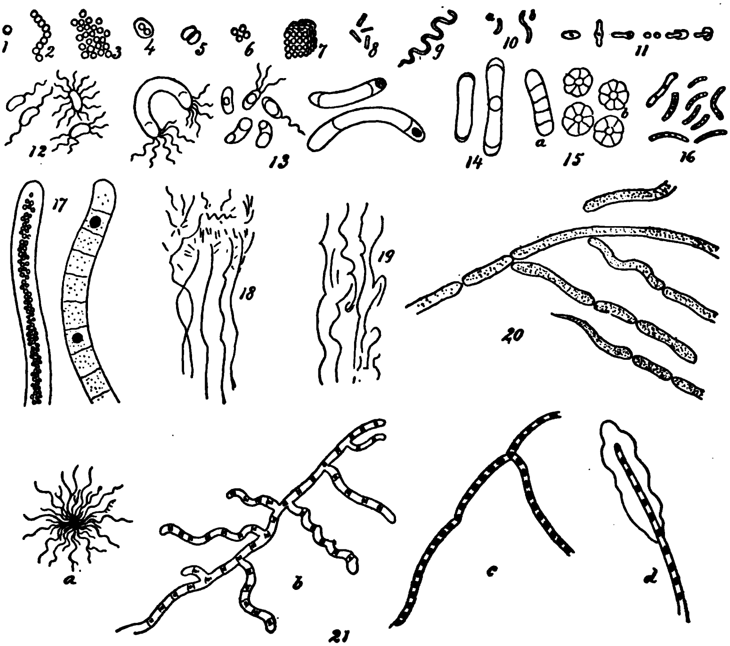


FIG. 59.—TYPES OF MICRO-ORGANISMS.

1, Coccus. 2, Streptococcus. 3, Staphylococcus. 4, Capsulated diplococcus. 5, Biscuit-shaped coccus. 6, Tetrads. 7, Sarcina form. 8, Types of bacilli (1 to 8 are diagrammatic). 9, Non-septate spirillum; ×1000. 10, Ordinary spirillum—(*a*) comma-shaped element; (*b*) formation of spiral by comma-shaped elements; ×1000. 11, Types of spore formation. 12, Flagellated bacteria. 13, Changes in bacteria produced by plasmolysis (after Fischer). 14, Bacilli with terminal protoplasm (Bütschli). 15, (*a*) Bacillus composed of five protoplasmic meshes; (*b*) protoplasmic network in micrococcus (Bütschli). 16, Bacteria containing metachromatic granules (Ernst Neisser). 17, Beggiatoa alba. Both filaments contain sulphur granules—one is septate. 18, Thiothrix tenuis (Winogradski). 19, Leptothrix innominata (Miller). 20, Cladothrix dichotoma (Zopf). 21, Streptothrix actinomyces (Boström), (*a*) colony under low power; (*b*) filament showing true branching; (*c*) filament containing coccus-like bodies; (*d*) filament with club at end.

Sporulation occurs when the conditions favoring multiplication no longer exist. There are then formed small, round, highly refracting bodies called *spores*, which are capable of resisting very unfavorable surroundings. They differ from bacteria in being able to withstand evaporation and quite high degrees of heat. Are called *endospores* when formed within the bacterium, may be in the middle or in one or both ends. When the spore is located in the center and distends the organism it is called a *clostridium*. If the entire organism is transformed into a spore it is known as an *arthrospore*.

Conditions concerned in the growth of bacteria are:

Food.—Proteids are best, but carbohydrates will do. Many pathogenic bacteria require special media upon which to grow.

Moisture is an almost absolute necessity. Unless it is present nearly all organisms will dry up and cease to multiply, but spores may first be formed and persist indefinitely.

Oxygen may or may not be necessary.

Micro-organisms which require the presence of uncombined oxygen are called *aërobic*.

Those not requiring but able to grow in it, *facultative aërobic*.

Those unable to grow in it, *obligatory anaërobic*.

Those able to grow without it, *facultative anaërobic*.

If able to grow equally well with or without oxygen, *optional anaërobic*.

Temperature is of the greatest importance. Every micro-organism grows best at some definite degree of heat and shows variations in its activity as the temperature changes. The organisms may, however, be able to endure extreme degrees of cold without being destroyed,—can be placed in liquid air and yet undergo multiplication when the temperature is raised. They cannot, however, stand the higher temperatures as well, although a few organisms may thrive at high degrees (65°–70° C.). They are the *thermophilic* bacteria and live in hot springs.

Bacteria growing between 0° C.–30° C. are psychrophile.
" " " 10° C.–45° C. are mesophile.
" " " 40° C.–70° C. are thermophile.

The pathogenic organisms grow best at a temperature normal to the body, 37° C.

A temperature of from 50° to 60° C. will weaken and finally destroy nearly all forms. If they are exposed to steam or boiling water at a temperature of 100° C., all bacteria will be killed in a few moments, but the spores are able to withstand this heat for some time. If there is no moisture present, 140° C. may be required before destruction takes place.

Reaction of the medium influences the growth, most organisms growing best in neutral or feebly alkaline media, although some grow well in strong acids and others in marked alkalinity.

Many chemical bodies will restrain the growth or destroy the bacteria. These bodies may be produced by the bacteria or they may be artificially introduced. Those which will restrain the growth but will not kill are called *antiseptics*. Those that kill, *germicides*.

Light, particularly the direct rays of the sun, will retard bacterial growth and in many cases kill the organism through the formation of H_2O_2. Blue rays are particularly effective.

Absence of *motion* seems more favorable to growth than rapid movement.

Electricity and *X-rays* do not seem to have any constant effect upon micro-organisms.

The *association* of one organism with another may cause an increase in its activity, as the growth of the tetanus bacillus in the presence of other bacteria that use up the supply of oxygen.

The reverse may be true: one organism may destroy another. The diphtheria bacillus may be killed in time by the action of bacillus pyocyaneus.

Products of Bacterial Growth.—Bacteria may be divided according to their products into:

Zymogens, bacteria of fermentation.
Saprogens, bacteria of putrefaction.
Chromogens, color-producers.
Photogens, phosphorescent bacteria.
Aërogens, gas-producers.
Pathogens, disease-producing bacteria.

Bacteria through their activity split up complex organic substances into simple ones.

In *fermentation* there is a splitting up of the carbohydrates. This is the process that takes place in the formation of alcohol as a result of the action of yeast.

Putrefaction is the breaking up of nitrogenous compounds. The albumins are first transformed into peptones which split up into gases, acids, bases, and salts. Both fermentation and putrefaction may result from the enzymes produced by bacteria.

The albumins may become changed into toxalbumins or into alkaloidal substances called *ptomains*.

"A *ptomain* is a chemical compound containing nitrogen, basic in character, formed by the action of bacteria upon organic matter." Ptomains are generally elaborated outside of the living body and cause harm only when introduced within it.

Toxins and *toxalbumins* are the poisonous substances elaborated by bacteria during growth, and it is upon them that the disease-producing power of the organism rests.

The toxins differ from the toxalbumins in that although proteid in character they do not give any of the albumin reaction.

The *bacterio-proteins* also belong to this same group. These bacterial products are destroyed by sunlight, by heating at 60° to 80° C., by long keeping, and by the gastric juices. Tuberculin is an exception; it can withstand 100° C. The poisonous bodies may be either soluble or insoluble and are generally peculiar to the variety of organism by which they are formed. Certain ones seem to select definite cells upon which to act, and are called *specific*. Others, having no special selective powers, are *non-specific*.

Toxins to cause disease must gain entrance to the blood. They are very powerful, $\frac{1}{275}$ of a grain of tetanus toxin being fatal to an adult. The combating of disease rests upon the power of the organism to resist the action of the poisons. If the power is enough to neutralize their effects, no symptoms will result. If the resistance is insufficient, disease will follow. Other products are:

Acids, acetic, butyric, lactic, etc.

Gases, HCO_2, H_2S, NH_4, etc.

Odors from aromatic substances, as indol, skatol, kresol.

Pigments, blue, red, orange, black.

Phosphorescence.

Reduction of nitrates.

Enzymes, which may cause fermentations, putrefaction, coagulation of milk, liquefaction of gelatin, etc.

CHAPTER XII

SPECIFIC MICRO-ORGANISMS

Staphylococcus pyogenes aureus is a non-motile, facultative, anaërobic coccus about 0.8 μ in diameter, occurring in groups or singly.

Stains with aqueous solutions of anilin dyes and by Gram's method.

It gives rise to pus-formation and to pyemia.

Culture.—On gelatin plates occurs as small whitish colonies, which cause liquefaction on the surface. The orange pigment is best seen in the center of the colony. In gelatin puncture it grows as a fine white line, developing its pigment in about three days. Liquefies the gelatin and gives an orange-colored precipitate. On agar there is considerable variation in the color; is rarely golden, commonly yellow, often cream color. Grows as a moist, shining, circumscribed colony; does not liquefy agar. On potato growth is luxuriant. Best temperature, 37° C.

Staphylococcus pyogenes albus is similar in every respect except that it does not produce any pigment.

Staphylococcus epidermidis albus is a micrococcus constantly present in the skin. Thought to be the S. pyogenes albus in an attenuated condition. Similar to the above.

Staphylococcus pyogenes citreus, similar, except that it produces a lemon-yellow pigment.

Streptococcus pyogenes is a non-motile, non-liquefying, facultative anaërobic coccus that is about 0.4 to 1 μ in diameter, that occurs in chains of 10 to 50 members.

Stains with ordinary dyes and by Gram's.

Is found in pus and in erysipelas.

Culture.—Best at 37° C. On gelatin plates small, colorless, transparent colonies develop in from twenty-four to forty-

eight hours. Are round, granular, with raised edges. Do not liquefy. On agar-agar have very delicate, transparent colonies that do not coalesce.

When it gains entrance into the body it gives rise to more diffuse and more severe suppurations than does the staphylococcus.

Bacillus pyocyaneus is an actively motile, flagellated, facultative, anaërobic, liquefying bacillus. Is rather short and slender, 0.3 $\mu \times$ 1 to 21 μ.

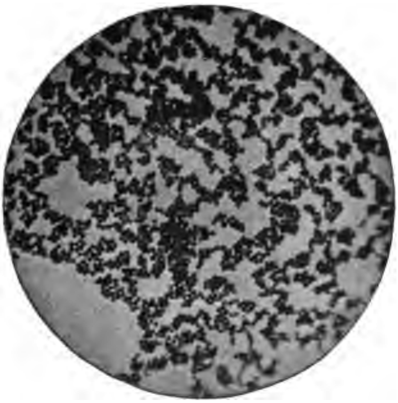


FIG. 60.—STAPHYLOCOCCUS PYOGENES AUREUS, FROM AN AGAR-AGAR CULTURE. $\times$ 1000 (Günther).

Stains.—Ordinary methods, but decolorized by Gram's. Is found in pus.

Culture.—On gelatin plates forms small, irregular, slightly greenish colonies. Produces a fluorescence of the neighboring gelatin. On agar-agar there is first produced a soluble bright green pigment along the line of inoculations. As the culture becomes older a second pigment forms, causing the medium to become a deep blue-green or dark blue.

Micrococcus gonorrhœæ is a non-motile, non-liquefying coccus found in pairs with slightly concaved surfaces opposed. From 0.8 to 1.5 μ in diameter.

Is a purely parasitic organism; is pathogenic for man only. Is found in the pus of gonorrhea, in the cells and also free in the serum.

Stains by ordinary methods but not by Gram's.

Culture.—Is difficult. Does not grow on any of the ordinary media. Human blood-serum is the best. On it the organism in about twenty-four hours forms isolated, thin, gray colonies that later on become confluent. Can be

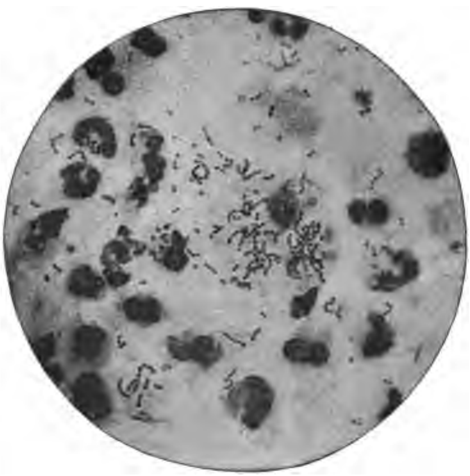


FIG. 61.—STREPTOCOCCUS PYOGENES, FROM THE PUS TAKEN FROM AN ABSCESS. × 1000 (Fränkel and Pfeiffer).

grown on gelatin that contains acid urine and also in plain acid urine.

It gives rise to suppurative inflammations of the mucous and serous membranes. May cause malignant endocarditis, arthritis, and salpingitis.

Diplococcus intracellularis meningitidis is a non-motile, non-liquefying, optionally anaërobic coccus, found usually in pairs, but may occur in short chains.

Is found within the protoplasm of the leukocytes.

Stains.—Ordinary ones and Gram's.

Culture.—Grows best at 37° C., but is not easily cultivated. Will develop on agar-agar, glycerin-agar, and in Loeffler's blood-serum. Growth is not characteristic; occurs as minute round grayish colonies that may coalesce. Requires frequent transplanting.

Diplococcus pneumoniæ is a minute, slightly lancet-shaped, non-motile, non-liquefying, optionally anaërobic diplococcus. Usually occurs in pairs, surrounded by a capsule that is not present when the organism is grown on culture medium.

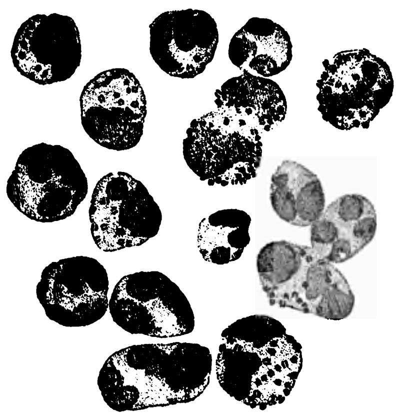


FIG. 62.—GONOCOCCI IN LEUKOCYTES; COVER-GLASS PREPARATION OF GONORRHEAL PUS (Warren).

Is found in the sputum of lobar pneumonia, in the exudate of meningitis, and sometimes in the saliva of healthy people. Is the common cause of croupous pneumonia, but is also found in inflammations of the serous membranes.

Stains.—Ordinary methods and Gram's.

Culture.—Grows best at 37° C., but has a range from 24° to 42° C. Will grow upon all culture media except potato. Gelatin plates (15 per cent. gelatin) give colonies that are small, round, circumscribed white points. On agar-agar the growth is almost invisible.

Bacillus tetani is a motile, flagellated, sporogenous, liquefying, obligatory anaërobic bacillus. Is found in earth, particularly that which has been manured, and in the discharges from wounds after infection. It is about 0.3 $\mu \times$ 2 to 4 μ in size, usually straight, but frequently club-shaped, due to the presence of a large round spore.

Stains.—Usual ones and Gram's.

Culture.—Will grow only when there is no free oxygen present. Grows best in alkaline gelatin that contains 2 per cent. dextrose. In stab cultures in gelatin and in agar-agar colonies form at right angles to the puncture. In gelatin liquefaction begins in the second week.

This organism is the cause of tetanus in man.

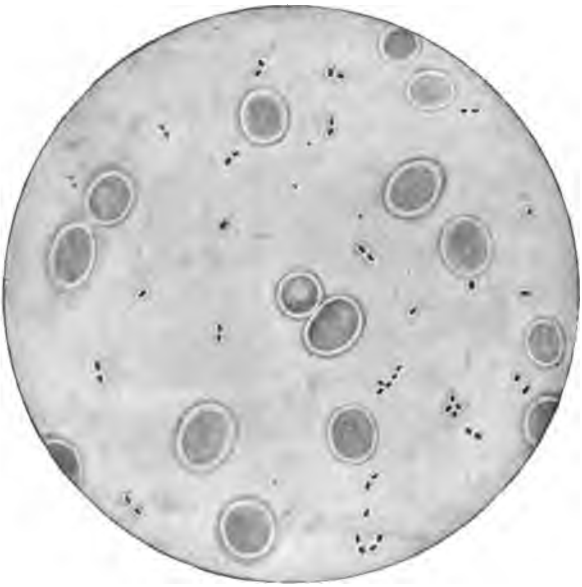


FIG. 63.—CAPSULATED PNEUMOCOCCI IN BLOOD FROM THE HEART OF A RABBIT; CARBOL-FUCHSIN, PARTLY DECOLORIZED. × 1000 (McFarland).

B. pneumoniæ is an encapsulated, non-motile, non-sporogenous, aërobic bacillus, so short that it may resemble a coccus. Varies, however, in length and sometimes occurs in chains of four or more individuals. Is found in the sputum and in the lung of croupous pneumonia.

Stains.—Ordinary methods, but not by Gram's.

Culture.—Ordinary media. In gelatin punctures gas-bubbles quite frequently appear, but there is no liquefaction of the medium. Gives the so-called "nail growth." Will grow from 16° to 40° C.

B. diphtheriæ is a non-motile, non-liquefying, aërobic organism from 0.4 to 1.0 μ broad, by 1.5 to 3.5 μ long, slightly curved and with clubbed ends. Is found in the pseudo-membranes of those suffering from diphtheria. It is peculiar in that in a pure culture there will be found individuals differing greatly in size and shape. These probably represent involution forms, as they are found in greatest numbers in old cultures.

FIG. 64.—BACILLUS OF TETANUS WITH SPORES (Fränkel and Pfeiffer).

Stain.—Ordinary methods, but particularly Loeffler's methylene-blue. Stains by Gram's. The ends take the stain more deeply than the middle.

Culture.—Ordinary media. Is obtained very easily in pure culture. The best medium is Loeffler's blood-serum mixture. On it there appears a smooth, smeary, yellowish-

white layer at the end of about twelve hours when grown at a temperature of 37° C. To make the diagnosis a swab of absorbent cotton is brought in contact with the suspected surface and the tube is then inoculated directly. A diagnosis can be made at the end of five hours. On gelatin the colonies appear as white points. On bouillon a distinct whitish pellicle forms on the surface. Also on agar, milk, and potato.

FIG. 65.—BACILLUS DIPHTHERIÆ, FROM A CULTURE UPON BLOOD-SERUM. × 1000 (Fränkel and Pfeiffer).

Pathogenesis.—When introduced into the individual it causes on mucous membranes the formation of a pseudomembrane, composed chiefly of fibrin but containing desquamated epithelium and B. diphtheriæ. Is generally associated with both staphylococci and streptococci, giving rise to a mixed infection. Besides the local lesion there is a marked and serious intoxication, resulting from the absorption of poisonous metabolic products.

Preparation of the Diphtheria Antitoxin.—Virulent diph-

theria bacilli are grown in alkaline bouillon containing 2 per cent. peptone for a period of three or four weeks at a temperature of 37° C. The culture is then heated for two hours at 65° C. and passed through a Chamberland filter. In this fluid there is the *toxin*. It is kept in sterile bottles in the dark.

For the purpose of immunization the horse is the best animal, as it furnishes a greater amount of antitoxic serum in less time than when a smaller animal is used. The horse is injected hypodermically with 0.1 c.c. of the toxic serum. In the course of six days a larger dose is given; this is repeated about every six days till from 500 to 1000 c.c. can be given without ill effects. When the degree of immunity is high the blood is withdrawn from a vein and collected in sterile bottles. These are placed on ice for about four days and the clear serum is drawn off from the coagulated blood. This serum is the *antitoxin*. It is preserved by the addition of 1 : 1000 formaldehyde, phenol, trikresol, carbolic acid, etc.

The strength of the serum is designated by the term "immunizing units." According to Ehrlich and Behring, the "normal serum" is so strong that 0.1 c.c. of it would protect against ten times the least surely fatal dose of toxin when simultaneously injected into a guinea-pig. At present the "immunizing unit" is considered as containing ten times the least amount of antitoxin that will protect a 300-gram guinea-pig against the action of ten times the minimum fatal dose of the toxin.

To determine the strength of any given serum the minimum fatal dose of a sterile toxin for a 300-gram guinea-pig must be ascertained. Then determine the least quantity of the antitoxic serum that will protect a guinea-pig against ten times the minimum fatal dose of the toxin. The necessary dose of antitoxic serum is expressed as a fraction of a cubic centimeter and multiplied by ten, the result equaling one unit.

The value of the antitoxin depends upon its use in the early stages, before the third day. It should be employed in doses of from 1000 units for a child to 2000 for an adult. Smaller doses may be used as a prophylactic in those who have been exposed to diphtheria.

In severe cases more than one injection may be necessary. Amelioration of the local and general symptoms indicates the favorable action of the serum.

B. anthracis is a non-motile, sporogenous, liquefying, aërobic bacillus, from 1 μ to 1.5 μ in breadth by 5 to 20 μ in length. Has square ends and is found either singly or in long threads. The organism is found in the blood of the infected animal as well as in the local lesions.

Stains by usual methods and by Gram's.

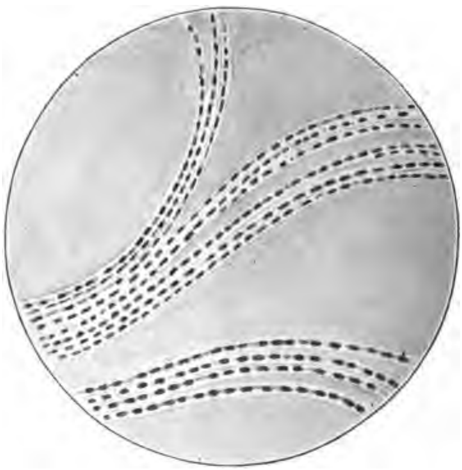


FIG. 66.—BACILLUS ANTHRACIS (Migula).

Culture.—Grows readily on all media. On gelatin surface colonies appear as small, round, grayish-white dots, accompanied by liquefaction. In gelatin stabs there is a characteristic tree-like growth.

Grows at temperatures from 12° to 45° C. Toward the higher point there is marked formation of spores which appear as oval, transparent bodies situated at the middle of the bacillus and not causing any alteration in its shape.

Pathogenesis.—Is the cause of anthrax, wool-sorter's

disease, or malignant pustule. It gains entrance by means of wounds, through the respiratory or through the alimentary tract. The viscera show marked congestion. Under the microscope numerous bacilli are seen in the capillaries.

Symptomatic anthrax is a motile, flagellated, sporogenous, anaërobic, liquefying bacillus about 0.5 μ in breadth and 3 to 5 μ in length, with rounded ends, found in the lesions of symptomatic anthrax.

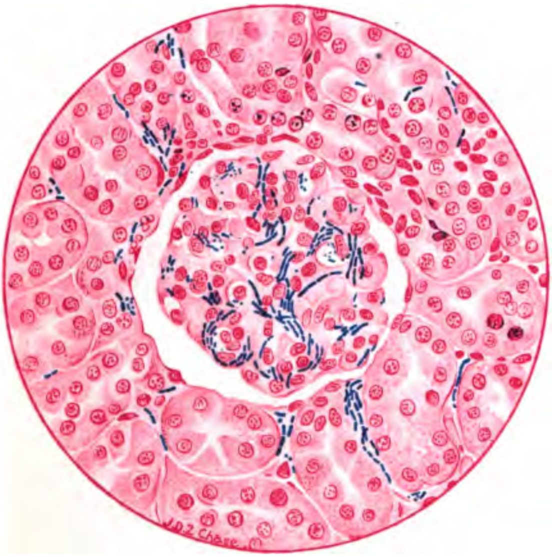


FIG. 67.—ANTHRAX BACILLI IN GLOMERULI OF KIDNEY (McFarland).

Stains.—Usual ones. Not by Gram's.

Culture.—Is strictly anaërobic. Liquefies gelatin, and in stabs forms gas. Colonies are spherical or slightly irregular in outline. Forms large oval spores that distort the organism.

Bacillus œdematis maligni is a motile, flagellated, anaërobic liquefying, sporogenous bacillus, 0.8 to 1.0 μ in breadth

and 2 to 10 μ in length, with rounded ends. Is found in garden earth, in the intestines of healthy animals, and in the lesions of the disease. Is not found in the blood on account of the oxygen present. May occur in long chains.

Stains.—Usual methods, but not Gram's.

Culture.—Ordinary media. On gelatin forms small, shining, grayish-white colonies. Under microscope can see long tangled filaments. In glucose-gelatin stabs forms white cloudy areas with some slight gas production.

FIG. 68.—BACILLUS INFLUENZÆ, FROM A GELATIN CULTURE. × 1000 (Itzerott and Niemann).

It is the cause of malignant edema. Is pathogenic for most animals, but cattle seem immune.

Bacillus influenzæ is a minute, non-motile, non-liquefying, aërobic bacillus found in the discharge from the nose and bronchi of those affected by influenza. Is also sometimes found in the blood. Is very small, about 0.2 × 0.5 μ, are usually single, but may occur in chains of three or four.

Stains.—Ordinary methods, but not by Gram's.

Culture.—Grows poorly on artificial media. Will not

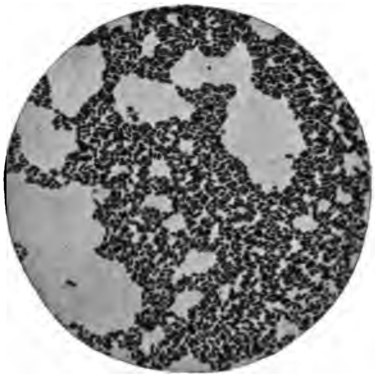


FIG. 69.—BACILLUS TYPHOSUS, FROM A TWENTY-FOUR-HOUR-OLD AGAR-AGAR CULTURE. × 650 (Heim).

FIG. 70.—BACILLUS TYPHOSUS, SHOWING FLAGELLA (McFarland).

grow at all on ordinary gelatin or agar-agar. Develops best upon media containing blood. Colonies appear as minute colorless bodies, looking like dewdrops. They do not coalesce. Is easily destroyed; 60° C. for five minutes will kill it. Will not grow below 28° C.

Bacillus typhosus is a motile, flagellated, non-sporogenous, non-liquefying aërobic, facultative anaërobic bacillus, 0.5 to 0.8 μ broad by 1 to 3 μ long, with rounded ends. Seldom seen in chains. Is found in the urine and feces of infected individuals; also in the blood, gall-bladder, and internal organs. Is present in water and milk as a result of contamination.

Stains.—Ordinary methods, but not by Gram's.

Culture.—Ordinary media. On potato there is formed a characteristic, thick, moist and shiny, invisible film.

Must be distinguished from the B. coli communis.

The following are the chief differences between the two:

	B. TYPHOSUS.	B. COLI COMMUNIS.
Colonies on gelatin plates:	On surface large, thin, and bluish, with notched border; yellow-brown in center. Deep colonies, brownish-yellow and sharply circumscribed. Non-liquefying.	On surface large, yellow-brown, round or oval with irregular border. Below surface round, yellow-brown, homogeneous. Non-liquefying.
On potato:	Usually forms a thick, moist and shiny, invisible layer. Sometimes yellowish or brownish.	Luxuriant growth. Yellowish-brown and glistening.
Milk:	Slightly acidulated but not coagulated. Diffuse cloudiness.	Rapid coagulation and acidulation. Turns blue litmus red, coloring medium. Marked turbidity.
Bouillon:	No indol.	Indol in twenty-four to forty-eight hours.
Ferments:	No gas formed in media containing sugar.	Fermentation whenever sugar is present.
Potassium nitrate:	Not reduced.	Reduced to nitrites and then to ammonia.
Neutral red:	Color remains.	Changes to yellow.
Widal test:	Positive with the serum of typhoid blood.	Negative.

B. coli communis.—See typhoid. Structurally it resembles the B. typhosus.

B. pestis.—A minute non-flagellated, non-motile, non-sporogenous, non-liquefying aërobic, and facultative anaërobic bacillus. Is very short, 1.7 μ by 2 μ, with rounded ends. Varies greatly in shape. Is found in the blood and in the enlarged lymphatic nodes.

Stains.—Ordinary methods, but not by Gram's. The rounded ends stain more deeply than the middle, giving an appearance of a diplococcus.

Culture.—Grows well on artificial media. Diffuse cloudiness in bouillon. Gelatin puncture growth scanty. On agar-agar forms white or bluish-white colonies with round uneven edges. On agar-agar plus 2.5 per cent. salt forms marked involution forms. Best medium for culture is a 2 per cent. alkaline peptone solution containing 1 or 2 per cent. of gelatin.

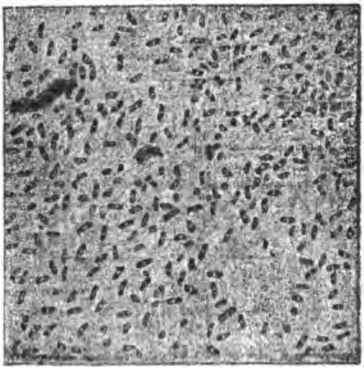


FIG. 71.—BACILLUS OF BUBONIC PLAGUE (Yersin).

Is the cause of bubonic plague in man. Is spread by means of rats and flies.

Bacillus aërogenes capsulatus.—A large non-motile, non-flagellate, sporogenous, purely anaërobic bacillus, 0.5 μ broad by 3 to 5 μ long, and with rounded or square ends. Occurs in groups and in pairs, but not in chains, in this way differing from the anthrax bacillus. Is found in the tissues in the necrotic areas.

Stains.—Ordinary methods and by Gram's. The organisms obtained from the body show distinct capsules.

Culture.—Ordinary media, but in glucose gelatin shows best the characteristic gas-production. Is no distinct liquefaction, but the gelatin becomes softer. In deep stabs

forms small, knot-like, grayish-white colonies from which extend fine hair-like or feathery projections. Produces acid.

Causes emphysematous gangrene with necrosis of the tissue before death and the formation of gas post mortem.

Spirillum choleræ asiaticæ is a motile, flagellated, non-sporogenous, liquefying aërobic, and facultative anaërobic spirillum; found in short arcs, spirals, and "comma" forms. About 0.8 μ long. Has a single end flagellum. Is found in

FIG. 72.—CHOLERA SPIRILLA, SHOWING FLAGELLA (Muir and Ritchie).

the feces, never in the blood or tissues, of those suffering from Asiatic cholera.

Stains.—Usual methods, but not by Gram's.

Culture.—Easily cultivated. On gelatin plates colonies appear in lower layer as small white dots. Extend to surface, causing liquefaction. Are granular. Gelatin stab cultures show liquefaction gradually extending from the surface downward. Gives rise to an inverted cone with an air-bubble at the upper end. In liquid media the presence of

indol and of nitrites is shown by the addition of one or two drops of chemically pure sulphuric acid, a reddish color being produced. Forms acid but does not coagulate milk.

FIG. 73.—SPIRILLA OF RELAPSING FEVER IN HUMAN BLOOD. × 1000 (Boston).

The spirilla resembling that of cholera are the following:

Finkler-Prior spirillum. — Similar in shape but shorter and stouter. Actively motile. Growth rapid. Does not

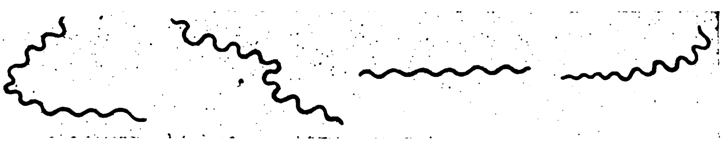


FIG. 74.—SPIROCHÆTA PALLIDA.

produce indol. Causes extensive liquefaction of gelatin. Is found in the feces of cholera morbus.

Vibrio tyrogenum.—Found in old cheese. Similar in form. Growth and liquefaction faster than S. cholera but less rapid

than Finkler. Is actively motile and has an end flagellum. Forms yellow, irregular, distinctly circumscribed colonies.

Vibrio Metschnikovi is a spirillum closely resembling that of cholera and is found in the feces of chicken cholera. Is somewhat thicker and shorter than the S. choleræ. Growth is very similar to that of the cholera spirillum but is slower. Not pathogenic for man, but kills chickens, pigeons, and guinea-pigs.

Spirillum of relapsing fever is a long, undulating, actively motile, flagellated spirillum, about 0.1 μ in diameter and 20 to 40 μ long. Non-sporogenous. Are found in the blood of patients during the height of the attack, but disappear after the temperature has fallen.

Stains by ordinary methods, but not by Gram's.

Culture.—Has never been grown outside of the body. Can be transmitted to monkeys by inoculating with infected blood.

Spirochæta pallida is an organism recently thought to be the cause of syphilis. It is very delicate, weakly refractile, and very motile. Is long, thin, spiral or corkscrew shaped, with pointed ends. Is from 4 to 10 μ long, 0.25 μ thick, and contains 6 to 14 turns, which are narrow and regular. This organism is difficult to stain; best results are derived from Giemsa's or Romanowsky's stains. Are difficult to find, both on account of their minuteness and their scarcity, few being found, as a rule, in a single preparation. They are found in the various primary and secondary lesions and in the blood, but not during the tertiary stages. Have not been artificially cultivated.

CHAPTER XIII

THE SPECIFIC GRANULOMATA

TUBERCULOSIS

Tuberculosis is a specific infectious disease characterized by the formation of tubercles.

Is caused by the B. tuberculosis, which is non-motile, non-sporogenous, aërobic, acid-resisting, and purely parasitic. Occurs as a slender, rod-shaped, slightly curved body, usually with rounded ends, but sometimes showing distinct branches. Is about 1.5 to 3.5 μ long, by 0.25 μ wide. Is found in sputa and in the lesion of tuberculosis. Is the cause of all forms of tuberculosis in man and may be transmitted to many of the lower animals. Is still unsettled whether the forms found in animals are capable of being pathogenic to man.

Staining is difficult, but after having once taken it up the organism is with difficulty decolorized. Use Ziehl-Neelson or Gabbett's method. Stains by Gram's.

Culture.—Blood-serum, glycerin agar-agar, potato, and glycerin bouillon. Growth is slow, best at 37° C., none when below 29° C. or above 42° C. Growth is dry, lusterless, coarsely granular, wrinkled, and slightly yellowish.

Pathogenesis.—Tuberculosis results from the successful invasion of the B. tuberculosis. This may take place by means of: (1) the respiration; (2) the blood circulation; (3) lymphatic channels; (4) by ingestion. After having gained entrance it may give metastases by any of the first three, by continuity of tissue, or by direct implantation.

The characteristic lesion is the miliary tubercle. It is a small area of inflammation and degeneration resulting from the action of the bacillus. When the organism enters a suitable location it undergoes multiplication. In a short time

their number and the products of their metabolism bring about an increase in the number of fixed connective-tissue cells, epithelioid cells. These cells are the first to appear. A little later, through the chemotactic effect of the bacteria, lymphoid cells escape from the blood-vessels. According to which cell predominates, the tubercle may be either *epithelioid* or *lymphoid*.

As the bacteria multiply more nutrition is required, but this variety of inflammation is peculiar in that not only no new blood-vessels are formed but the pre-existing ones are destroyed as the process advances. Consequently the central area undergoes degeneration and coagulation necrosis.

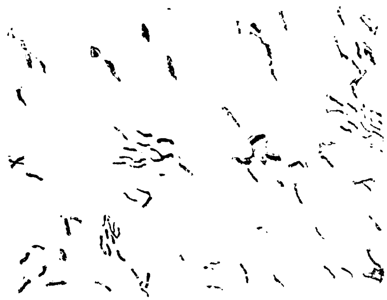


FIG. 75.—TUBERCLE BACILLI IN SPUTUM (Ziegler).

The tubercle may be divided into three zones, according to its histologic characteristics: (1) A *central* zone containing degenerated tissue cells and bacteria. (2) A *median* zone, in which are many epithelioid cells and frequently giant cells containing vesicular nuclei arranged peripherally and radially. (3) A *peripheral* zone, in which are found a few epithelioid and many lymphoid cells.

The giant cells as well as the epithelioid may come from the endothelium of the blood-vessels or lymph-vessels, from fibroblasts or from escaped leukocytes.

If the process has been rapid the lymphoid cells usually predominate. If the individual's resistance is fairly good, some of the epithelioid cells may be converted into fibrous tissue. When resistance is marked, the tubercle may become encapsulated by fibrous tissue and eventually become infiltrated by lime salts. This occurs only where the resisting power of the patient becomes greater than the destroying ability of the organism.

As, however, the bacilli keep continually multiplying the tendency of the disease is to extend. This occurs by the organisms being carried into the lymphatic channels either directly or by the action of phagocytes. The latter may carry and deposit them in a neighboring lymph-gland where secondary lesions will occur. Metastasis may also take place by the organisms gaining entrance into a vein, entering the

FIG. 76.—SUBACUTE TUBERCULOSIS OF A LYMPH-GLAND. × 70 (Dürck).
1, Thickened capsule; 2, caseous centers of the tubercles. At the periphery of the gland the tubercles are still discrete, and between them lies lymphadenoid tissue. In the center of the gland the nodules have formed larger confluent areas. Numerous giant cells.

general circulation and setting up a more or less widely diffused general miliary infection.

Recovery from tuberculosis is more common than is generally believed. According to post-mortem examinations, 20 per cent. of the cases of tuberculosis recover. In such cases there is present the ability of the individual to resist the inroads of the process. The tubercle bacilli become

encapsulated in a mass of connective tissue that prevents their further growth and extension. This new-formed tissue tends to contract and causes the broken-down portions to be absorbed, or else calcareous infiltration takes place.

These walled-off areas are, however, still a source of danger. Although tubercle bacilli do not form spores, yet infection may take place years after the connective-tissue growth, if for any reason the contents happen to escape.

When it remains quiet it is called "latent" tuberculosis.

The symptoms seen are probably due in a great part to the presence of associated pyogenic organisms, as no important toxic body has ever been obtained from the bacillus. The night-sweats, fever, and loss of weight seen in cases of pulmonary tuberculosis are due to the associated bacteria. There is generally present some anemia, and many authors claim that there is an increase in the number of lymphocytes in the blood.

The liver frequently shows marked fatty infiltration and sometimes amyloid degeneration to a slight or a marked degree.

The most common entrance for infection is the respiratory system. Sputum from tubercular patients becomes dried and comminuted; it is then carried about by the currents of air and enters the body.

The intestines may become secondarily involved through infection brought about by swallowing the tubercular sputum.

Congenital tuberculosis may come from the paternal side from infection of the genitals; from the maternal side through infection of an ovum, or it may be transmitted through the placenta. Heredity is no longer thought to have much direct influence. It is now believed that what is inherited is nothing more than a weakened resisting power.

LEPROSY

Leprosy is a chronic, specific, infectious inflammatory disease caused by the B. lepræ; which is a non-motile, non-sporogenous, acid-resisting, purely parasitic organism. Is pathogenic only for man. Is very slightly contagious. Is

stained with some difficulty. Stains by Gram's. It cannot be grown on artificial media.

It occurs most commonly in warm climates and in people of almost any age. Is most common in males of from twenty to thirty years. It is probably not hereditary, but children under three years have been affected.

The bacilli are distributed to an extraordinary extent in the body of the leper, and in many cases there will be no inflammatory reaction in their neighborhood. They may be either extracellular or intracellular, and in the latter case may be found in giant cells or lepra cells. These may contain numerous nuclei and numbers of vacuoles as well as bacteria.

The secretions of the mucous membranes of the nose usually contain great numbers of the bacilli.

FIG. 77.—GIANT CELL FROM A LEPROUS ULCER OF THE EPIGLOTTIS, SHOWING THE LEPRA BACILLI SCATTERED THROUGH THE TISSUE AND ENCLOSED IN A LARGE "LEPRA CELL" (Lehmann and Neumann).

Varieties.—Two forms are commonly met with, the *nodular* and the *anesthetic* or *nerve* leprosy. It is seldom, however, that a quite pure case of either is found; the majority belong to the mixed form. In the *nodular* variety the node may be preceded by a hyperemic patch which leaves behind it a pigmented area. The nodules appear first in the skin and subcutaneous tissue of the face, and may remain single or become confluent.

Macroscopically the nodes are rather grayish or yellowish. Microscopically they are composed of great numbers of small, frequently vacuolated epithelioid cells with also connective-tissue cells. These lesions are more vascular than those of tuberculosis, and consequently do not tend to undergo coagulation necrosis. Caseation does not take place and the ulceration that is so common depends largely upon injuries and secondary infections.

The nodules are found in other parts of the body, as on the back of the hand,—palm is not usually involved,—in the mucous membrane of the eye, nose, mouth, larynx, and intestine.

The lymph-glands in both varieties are swollen, hard from connective-tissue formation, and yellowish on account of fatty degeneration.

Anesthetic leprosy is characterized by the growth of the

FIG. 78.—NODULAR LEPROSY.

bacilli in the sheath of the nerves and an increase in the connective tissue along their course. Is most common on the ulnar and popliteal nerves. There then appears neuritis with localized hyperemic spots. These become anesthetic and in some cases become the seat of a blister. Finally ulceration may develop with the subsequent loss of the fingers or toes.

Many of the enlarged glands may be the result of a secondary tuberculosis occurring late in the course of the disease. There is frequently fever and also nephritis. Amyloid degeneration is not uncommon in the ulcerative forms.

The majority of the cases last from five to twenty years, usually dying of tuberculosis.

FIG. 79.—MACULAR LESIONS IN LEPROSY.

GLANDERS

Is a specific infectious disease of horses that is sometimes seen in man as the result of accidental infection.

Is caused by the Bacillus mallei, a non-motile, non-spor-

ulating, aërobic or optionally anaërobic bacillus. Is pathogenic for man and lower animals. Stains by ordinary methods, but not by Gram's.

It makes its appearance in the membrane of the nose in horses in the form of small nodules the size of a pea. These may increase in size, but eventually break down and ulcerate with the formation of irregular ulcers, having yellowish, elevated, and indurated borders from which some bloody pus is discharged. Lymph-glands become enlarged,

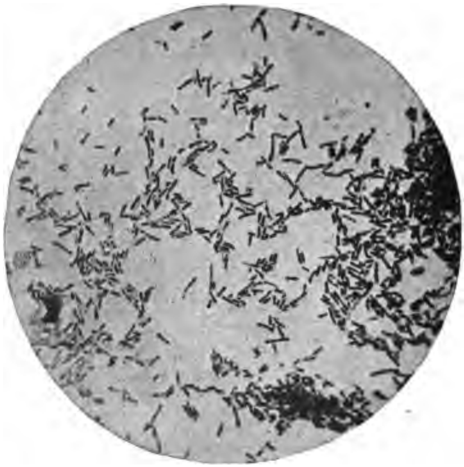


FIG. 80.—BACILLUS MALLEI, FROM A CULTURE UPON GLYCERIN AGAR-AGAR × 1000 (Fränkel and Pfeiffer).

and metastatic abscesses may result. The lungs are frequently involved.

Microscopically the nodules consist of masses of small round cells and epithelioid cells. Do not find giant cells.

If the skin is involved the condition is known as "farcy," and the nodules as "farcy buds." They generally undergo marked and extensive ulceration.

Man may become infected through lesions of the mucous

membranes of the eye or nose or of the skin, and the result is usually fatal.

ACTINOMYCOSIS

Is a chronic contagious disease of cattle, but is sometimes found in man.

Is caused by a fungus, the *Actinomyces bovis*, which is large enough to be seen by the naked eye, appearing as small yellow particles. The fungus is made up of a central mass of granular substance in which are many structures resembling chains of cocci or spores. Extending from this center are many mycelial threads terminating in club-shaped extremities. Is both aërobic and anaërobic in its growth; the latter form alone being pathogenic. Will grow on any artificial media.

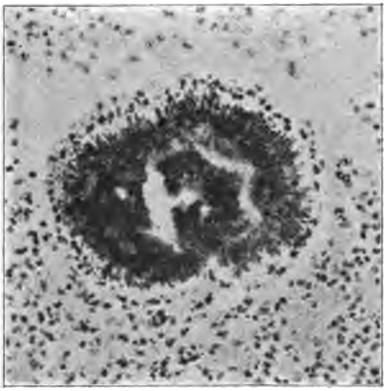


Fig. 81.—Actinomyces Cluster showing Radial Striations at Periphery (Karg and Schmorl).

Stains yellow with picric acid, red with picrocarmin, blue with anilin gentian and by Gram's.

The infection is supposed to take place by means of spores gaining entrance into the human system by means of food, or by inhalation. Probably enters by way of decayed teeth.

Where the fungus lodges there is a formation of nodules which break down, form abscesses, and discharge a creamy pus containing yellowish granules; which show the characteristic rayed appearance when looked at under the microscope.

The neighboring bones may become riddled and there may also be metastatic growths in other organs, particularly the lungs. In the latter extensive necrosis may occur and the fungus will be found in the sputum.

Instead of breaking down connective tissue may be formed and encapsulate the invaded area.

The characteristic lesion is the formation of embryonal connective tissue and granulation tissue.

MYCETOMA

Mycetoma or *Madura foot* is a chronic specific inflammatory condition caused by the *Actinomyces maduræ.* This organism closely resembles the A. bovis, but the club-shaped

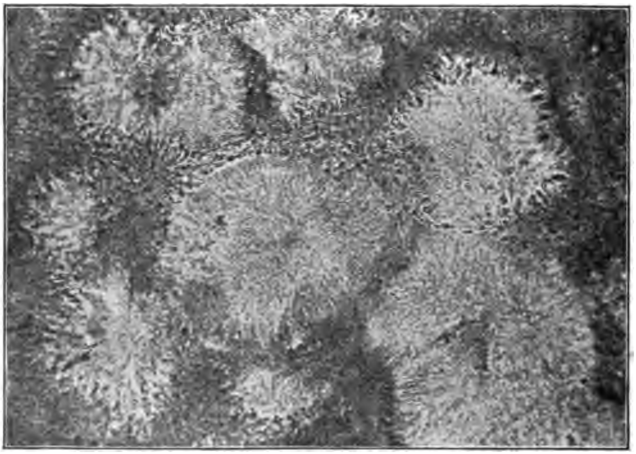


FIG. 82.—ACTINOMYCES OF MADURA FOOT (Wright and Brown). Granule crushed beneath a cover-glass, showing radial striations in the hyaline masses. Preparation not stained; low magnifying power.

extremities are absent and spores may occur along the threads. Can be grown artificially, stains by the ordinary methods and by Gram's.

Usually attacks the feet. A nodule slowly appears and in the course of a year or two may soften and discharge a thin pus in which are found minute rounded bodies resembling fish roe. These bodies may be either pinkish in color,

the *pale* or *ochroid* variety, or black like gunpowder, the *melanoid* form.

On account of the degeneration numerous sinuses may form. The disease is painless and seldom fatal.

MYCOSIS FUNGOIDES

Is a rare infectious disease of the skin and mucous membranes, possibly due to a protozoa, but the true cause is not known.

It makes its appearance as an erythema or eczema with the subsequent formation of a node below the surface. This node is quite red, hard, and sometimes painful. Softening at the top of the nodule takes place with extensive ulceration and the escape of a clear or blood-stained fluid. The appearance is said to resemble that of a tomato. There is seldom any attempt at healing, the ulcer increasing in size.

Microscopically there is found a marked formation of granulation tissue about the new-formed blood-vessels. Are numerous lymphocytes, epithelioid, and small giant cells. The poor blood-supply is probably the cause of the softening and ulceration.

MOLLUSCUM CONTAGIOSUM

Is probably a parasitic disease of the skin, as it is undoubtedly contagious, often occurring in small epidemics.

On the skin are found numerous papular or warty nodules about the size of a pea, later becoming larger, with a central saucer-like depression due to degeneration.

Microscopically the growth is made up of degenerated epithelial cells and small oval bodies, that may be either intracellular or extracellular. Each lesion is made up of a number of conical lobes converging toward a central opening. The cells may undergo an extreme cornification.

The peculiar transparent oval bodies are by some considered to be sarcosporidia, but the majority hold that they are degenerated epithelial cells.

RHINOSCLEROMA

Is a chronic infectious disease of the skin and of the nasal mucous membranes. Probably due to the *Bacillus rhinoscleromatis*.

The disease occurs in the form of small firm nodules made up of a dense cellular infiltration of the corium and papillary layer of the skin. New connective tissue continues to form and frequently a hyaline degeneration occurs.

The bacilli are found in the nodes either intracellular or extracellular.

SYPHILIS

Is a specific, infectious, and very contagious disease of man. Has never been observed in any of the lower animals except in the anthropoid apes.

Its etiology is uncertain, is possibly due to Lustgarten's bacillus, one that quite closely resembles the tubercle bacillus. More recently a spirillum, the *Spirochæta pallida*, has been so constantly found in syphilitic lesions that it seems very probable that that organism is the causative factor.

The disease may be divided into the:

1. Period of primary incubation, about three weeks.
2. Period of primary symptoms, chancre and adenitis.
3. Period of secondary incubation, about six weeks.
4. Period of secondary symptoms, from one to three years.
5. Intermediate period of two to four years, during which the patient may recover.
6. Period of tertiary symptoms, unlimited.

The **primary lesion** is the *chancre*, which starts as a single papule, seldom multiple, at the seat of inoculation, which may be either *genital* or *extragenital*. This soon becomes eroded, but increases in size due to infiltration of the deeper tissues. The base becomes hard, and the surface is either dry or is covered by a slight false membrane.

Histologically there is an infiltration of round cells, particularly along the vessels. Polymorphonuclear leukocytes, lymphocytes, plasma cells, endothelial and connective-tis-

sue cells, and fibroblasts are present. The blood-vessels undergo an arteritis, the endothelium is increased in thickness, and obstruction may occur. There is also frequently a hyaline change in the vessels.

The **secondary lesions** are first a swelling and induration of the neighboring lymph-nodes. There then appears a skin eruption accompanied by fever, constitutional symptoms, and a rapid decrease in the erythrocytes, with a moderate leukocytosis, usually of the lymphocytes. The skin lesions are generally symmetric, do not itch, and are coppery in appearance. May be some loss of hair.

The *mucous patch* or *condyloma latum* appears on the mucous membrane. It is a slightly elevated, moist, grayish lesion, covered by a thin pseudomembrane. In these there is round-cell infiltration of the skin with superficial necrosis. There may be one or more patches.

FIG. 83.—UPPER MEDIAN INCISORS IN HEREDITARY SYPHILIS (Cornil and Ranvier).

FIG. 84.—SERRATIONS IN NORMAL TEETH (Cornil and Ranvier).

Although the chancre and the secondary lesions are highly contagious the mucous patch is probably the most so.

The chief **tertiary** lesion is the *gumma*. It is found most commonly in the bones, in the liver, lungs, kidney, heart, and brain. The gumma is a nodular mass made up of granulation tissue in which are numerous blood-vessels. It usually undergoes a caseous or other form of degeneration, and may ulcerate or undergo cicatrization. It is hard, dense, and elastic.

The blood-vessels show an endarteritis which closes or narrows the lumen. The remains of broken-down cells and particles of fat are present and giant cells may be found.

Hereditary syphilis may result from disease of the ovum, spermatozoön, or both, or it may be transmitted through the placenta after conception has taken place.

The mother of a syphilitic child will be immune to the disease, although she herself shows no symptoms (Colles's law).

An apparently healthy baby born of a syphilitic mother cannot subsequently be infected by her (Profeta's law).

The fetus may die *in utero* and be aborted, the child may be born dead, or it may be alive but die shortly after birth.

The primary lesion does not occur in the hereditary form, but the secondary and tertiary manifestations may be evident, such as skin eruptions and mucous patches or even gummata.

The upper incisors of the second dentition are frequently conical and peg-shaped with deep notches at the free edge (Hutchinson's teeth).

There also frequently occurs a "white" pneumonia, cirrhosis of the liver, spleen, and pancreas, osteochondritis, and interstitial keratitis.

CHAPTER XIV

PARASITES

A *parasite* is an organism that lives in or upon another. Many are harmless, but some of them are distinctly pathogenic, as they live at the expense of the individual, to the detriment of its well-being.

The body at whose expense the parasite lives is called the *host.*

Parasites may be divided into the *vegetable* and the *animal* varieties.

Parasitic diseases are characterized by having a specific exciting cause and by the fact that they can be transferred from one individual to another. Some forms go through a portion only of their life history as parasites.

Others are able to live without the host and are known as *optional* parasites. To this class belong many of the insects.

Some cannot live independently and are known as *obligatory* parasites, such as the tapeworms. They have no sense-organs, alimentary tract, or circulation. They have no need of such structures, as their food is taken up by absorption. The organs by which they retain their grasp and their powers of reproduction are well developed.

Pathologic conditions due to parasites may be the result of *mechanical* or *chemical* phenomena.

Mechanical, as obstruction of the lumen of an intestine, vessel, or duct; hemorrhage resulting from bites and suction, pressure.

Chemical: disturbances resulting from the absorption by the host of poisons, or from degenerative processes, causing reflex nervous symptoms, inflammation, and irritation.

ANIMAL PARASITES

Protozoa.

Amœba coli.
Amœba dysenteriæ.
Coccidium oviforme.
Trichomonas intestinalis.
Cercomonas intestinalis.
Trichomonas vaginalis.
Plasmodium malariæ.
Yellow fever.
Trypanosomes.
Pyrosoma.

Flat-worms. Platyhelminthes.

Cestodes. Tapeworms.

Tænia solium.
Tænia saginata or mediocanellata.
Dibothriocephalus latus.
Tænia echinococcus.
Tænia nana.
Tænia cucumerina.

Trematodes. Sucking worms.

Distoma hepaticum.
Distoma lanceolatum.
Distoma hæmatobium.
Distoma pulmonale.

Nematodes. Round-worms.

Ascaris lumbricoides.
Oxyuris vermicularis.
Eustrongylus gigas.
Filaria medinensis.
Filaria sanguinis hominis.
Uncinaria duodenale.
Uncinaria americana.
Anguillula intestinalis.
Trichina spiralis.
Tricocephalus dispar.

PROTOZOA

Amœba Coli.—Probably two varieties, *Amœba coli communis*, non-pathogenic, and the *Amœba coli dysenteriæ*, the cause of dysentery.

Is found in the intestines, and in secondary abscesses, particularly of the liver.

Is a single spherical cell about 20 to 30 μ in diameter. Has no distinct membrane; each cell contains a nucleus and usually several vacuoles. The protoplasm is finely granular, frequently contains red cells and bacteria. The

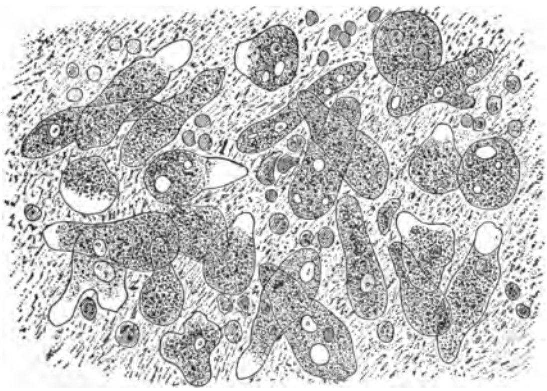


FIG. 85.—AMŒBA COLI IN INTESTINAL MUCUS, WITH BLOOD-CORPUSCLES AND BACTERIA (Lösch).

ameba is capable of moving by means of pseudopods. Ulceration of the intestine with perforation may occur. Sometimes find encysted forms.

Coccidium oviforme is an elliptical parasite that is rarely found in the intestines and liver of man but is common in rodents. It has a distinct double capsule, is found within cells in which it undergoes rapid division. Frequently becomes encysted, and when taken into the intestine the capsule is dissolved and the organism is set free.

Other less important parasites are the **Paramœcium coli,** an ovoid, unicellular organism about 7 to 10 microns long. Is surrounded by short cilia. Usually contains numerous large vacuoles. Is found in diarrheal feces.

The **Trichomonas intestinalis** is a pear-shaped organism about 10 to 15 microns long. On one side it has an undulating

FIG. 86.—COCCIDIOSIS OF RABBIT'S LIVER (McFarland).

Section of one of the affected bile-ducts, showing the papillary outgrowths from the mucous membrane and the signs of inflammation in the surrounding tissue.

membrane provided with about 10 to 12 cilia. Is found in intestinal discharges in diarrhea, typhoid fever, and cholera.

The **Cercomonas intestinalis** is a pear-shaped para-

PLATE I.

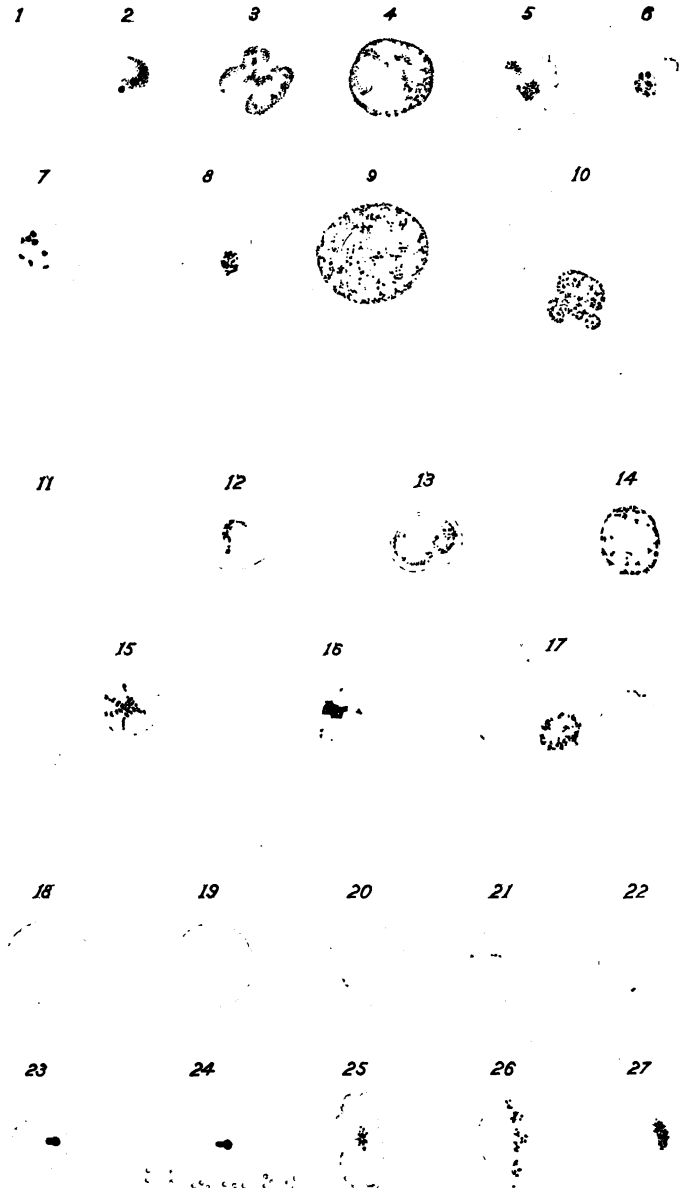


PLATE I.

VARIOUS FORMS OF MALARIAL PARASITES (Thayer and Hewetson).

Figs. 1 to 10, inclusive, tertian organisms; Figs. 11 to 17, inclusive, quartan organisms; Figs. 18 to 27, inclusive, estivo-autumnal organisms.

FIG. 1.—Young hyaline form; 2, hyaline form with beginning pigmentation; 3, pigmented form; 4, full-grown pigmented form; 5, 6, 7, 8, segmenting forms; 9, extracellular pigmented form; 10, flagellate form.

FIG. 11.—Young hyaline form; 12, 13, pigmented forms; 14, fully-developed pigmented form; 15, 16, segmenting forms; 17, flagellate form.

FIGS. 18, 19, 20.—Ring-like and cross-like hyaline forms; 21, 22, pigmented forms; 23, 24, segmenting forms; 25, 26, 27, crescents.

site about 10 to 12 microns long. From its blunt end extends a single flagellum.

The **Trichomonas vaginalis** is an oval organism about 10 microns long. To one end are attached three long flagella, near the base of which is an undulating membrane provided with five to six cilia.

It has been found in the urine as well as in the vagina.

The **Plasmodium malariæ** is a unicellular parasite that during one cycle of its existence lives in the blood and brings about a destruction of the erythrocytes. Its other cycle is carried on within the body of a mosquito, the Anopheles.

There are three varieties of the organism:

1. The *quartan* parasite attains its development in three days. It appears inside an erythrocyte as a small, unpigmented, irregular, hyaline body capable of slow ameboid movement. It grows gradually and brownish or black granules appear. The erythrocyte becomes gradually paler and is finally completely filled by the plasmodium.

The pigment occupies the center of the cell and later the parasite splits up into from six to twelve pear-like segments which, along with the pigment, escape into the circulation. Is the rosette form. The granules in this form are larger and darker than in the tertian, but not so numerous.

Double infection may occur, in which case there would be paroxysms for two days, then an intervening free day.

2. The *tertian* parasite requires two days for its development. In its early stages it resembles the quartan parasite, but it eventually becomes larger. The tertian continues growing till it may be double the size of the red cell, the pigment particles collect in the center, and the organism divides into fifteen to twenty small, round, spore-like bodies, resembling a bunch of grapes. This form of parasite contains more granules than the quartan, but they are smaller and the red corpuscle is rapidly decolorized.

3. The *æstivo-autumnal* parasite is probably a tertian form. Is sometimes spoken of as malignant tertian.

The cycle of development lasts forty-eight hours. The organism is smaller than in the first two, but more active. When fully developed it is about one-third the size of the red cell.

When at rest it assumes the signet-ring form, a disc with a colored outline. The pigment is very fine and hard to recognize. Is more marked in fresh specimens.

The organism finally becomes lobulated, rosette-shaped with the pigment in the center or toward the periphery, and divides into six to twelve little balls.

The development of this form seldom takes place in the peripheral blood, usually in the spleen, bone-marrow, and cerebral capillaries.

The erythrocytes tend to shrivel and become dark. In this variety of infection are found the *crescents* of Laveran. They are oval or crescentic bodies that are pigmented in their center and have no ameboid motion, but are able to slowly alter their shape.

When fully developed are larger than a red cell. They are found partly in red corpuscles, or clinging to them, free in the blood and sometimes in leukocytes. Occur only in the severe forms of malaria; are probably malignant tertian parasites that have failed to sporulate.

Flagellated bodies are found in all forms of malaria. They are small, spherical, pigmented bodies, about the size of an erythrocyte. They lie free in the blood and have from one to four long, delicate, actively motile flagella.

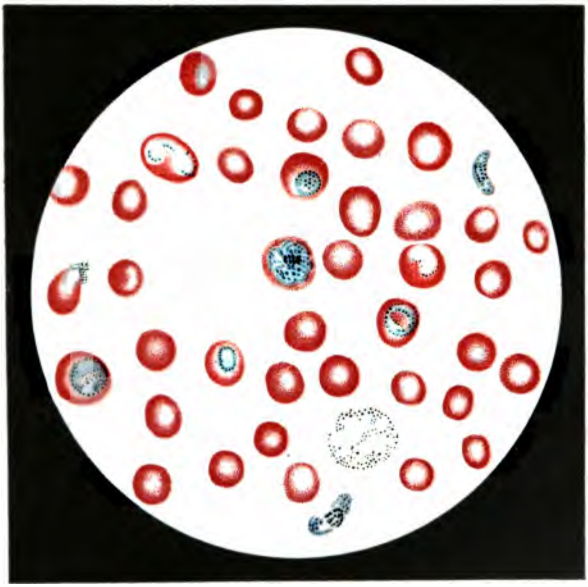
This form is not seen immediately after the removal of the blood, usually does not appear for some fifteen minutes.

They originate from the large pigmented spheres that have not sporulated, and represent the form of parasite that propagates the species outside the human body.

DIFFERENCES BETWEEN THE PARASITES.

Quartan.	Tertian.	Æstivo-autumnal.
Cycle three days.	Forty-eight hours.	Forty-eight hours.
Ameboid motion sluggish.	Rapid.	Brisk.
Red cell slowly decolorized.	Rapidly.	Cell becomes darker, bronze-like.
Little change in size of red cell.	Much swollen.	Cells small and shriveled.
Parasite sharply outlined.	Indefinite.	Faint.
Pigment granules coarse and few, and in rapid motion.	Fine and numerous; in motion.	Granules fine, not often in motion.
Spores six to twelve, large and pear-shaped.	Fifteen to twenty, small, round.	Six to twelve small spheres present.

PLATE II.



Malarial Parasites in Blood (Grawitz).
Numerous pigmented parasites, spore formation of the tertian type, and two crescents.

When the organisms sporulate and are set free within the blood the fever rises and the chill takes place. The escaped spores enter other red corpuscles, go through the same cycle, and a continuous reinfection occurs.

The foregoing cycle is the asexual one that takes place within the human body. It is now definitely settled that infection takes place by means of the bite of a special variety of mosquito, the Anopheles. Of mosquitos, only the female bites.

This insect withdraws the malarial parasites from an infected individual, they undergo further stages of development, and are again transmitted to other people by the mosquito biting.

In the blood of an infected person two chief forms of parasite are found. One that is the smaller is round and contains numerous granules and is called the *microgametocyte.* From it flagella are given off. These flagella penetrate a larger spherical form that has a clear protoplasm, the *macrogametocyte;* the former being the male, the latter the female element. The impregnated parasite is called a *zygote.* These zygotes penetrate the stomach and become attached to the outer wall, where they grow much larger and are called *sporozoöns* or meres. They finally undergo division into secondary spheres which ultimately split up into very many small spindle-like bodies known as *sporozoites* or blasts. These escape into the body cavity of the mosquito and the majority finally gain entrance into the salivary glands, from which they escape in the secretions.

When the blasts gain entrance into the blood they attack the red corpuscles and give rise to malaria.

In this case the mosquito is the definitive host of the parasite, man the intermediate.

The cycle of development in the mosquito takes from eight to ten days.

The following is a description of the Anopheles mosquito. Palpi in both sexes nearly as long as the proboscis, 4 jointed in female, 3 in male. Is a constricted basal joint in each.

Palpi are straight and parallel with proboscis except when female is biting, when they diverge.

Nucha has scaly posterior cornu, abdomen hairy on both surfaces, not scaly. Legs long and end in simple dentate claws. Wings spotted, and these spots when magnified are seen to be made up of black squamæ on brownish wing.

Length of female 7.5 to 9 mm., including proboscis; male smaller and does not bite.

When resting on a perpendicular wall the Anopheles extends its body at right angles unless it is filled with blood, the Culex holds its body parallel.

Yellow fever is an infectious disease, probably caused by some protozoon which is carried by a mosquito, the *Stegomyia fasciata.*

The female mosquito is from 3.5 to 5 mm. long, head clothed with flat scales, black and gray on each side. A white patch in the middle in front, extending back to the neck. A white patch on each side and thin white borders to the eyes. Antennæ blackish with narrow pale bands. Last joint of palpi white on inner side. Thorax dark brown, ornamented with white curved band on each side of the back and white spot on each side in front.

Abdomen dark with basal bands of white.

Fore- and mid-ungues toothed, hind ones not.

This mosquito may convey yellow fever to a non-immune as early as on the twelfth day after biting an infected person, and it may retain the power to do so as long as it lives.

This disease can also be transmitted by the hypodermic injection of blood drawn from a patient in the first, second, or fourth days of the disease. It cannot be communicated by fomites.

The infected agent can be passed through a filter that is impermeable to ordinary bacteria and is destroyed by a temperature of 55° C. maintained for ten minutes.

One attack usually renders a person immune.

Trypanosomes are elongate spindle-shaped organisms, a little longer than the diameter of a red corpuscle. One end terminates in a long flagellum. These bodies are found

in the blood in certain diseases of the lower animals, as "nagana" or tse-tse fly disease, or in "surra."

Recent investigations have shown the presence of trypanosomes in the cerebrospinal fluid of people suffering from "sleeping sickness."

Except in "dourine," in which the disease is transmitted among animals by coitus, a biting fly is the carrier of the infection.

Texas fever is an acute febrile disease of cattle resulting from the presence in the blood of the *pyrosoma bigeminum.*

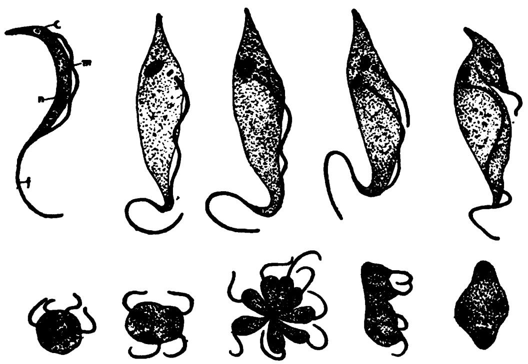


FIG. 87.—TRYPANOSOMA, SHOWING MULTIPLICATION BY DIVISION (from Laveran).

n, Nucleus; *c*, centrosome; *m*, undulating membrane; *f*, flagellum.

Is a small pear-shaped organism found within the red cells. In this disease the common cattle tick is the means by which it is spread. This parasite is peculiar in that it passes into the eggs of the tick and infects the embryos.

Montana spotted fever is a peculiar acute febrile disease found in a certain part of Montana and supposed to be caused by a blood parasite resembling the pyrosoma of Texas fever. Is thought that it is transmitted by woodticks that have first obtained blood from a variety of squirrel.

WORMS

Cestodes or **tapeworms** are more or less elongated, flattened, and segmented bodies that attach themselves to the mucous membrane of the intestine by means of suckers or hooklets.

FIG. 88.—HEAD OF TÆNIA SOLIUM (Mosler and Peiper).

FIG. 89.—MATURE SEGMENTS OF TÆNIA SOLIUM (Mosler and Peiper).

They have no alimentary canal. Are hermaphroditic. One cycle of their life-history is in man, the other in some

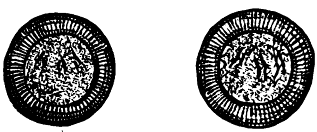


FIG. 90.—EGGS OF TÆNIA SOLIUM (Mosler and Peiper).

one of the lower animals. The fully developed worm is called a *strobile*. It consists of a head, a very narrow neck, and a number of segments called *proglottides*. These seg-

FIG. 91.—TÆNIA SOLIUM (Mosler and Peiper).

FIG. 92.—HEAD OF TÆNIA SAGINATA (Mosler and Peiper).

FIG. 93.—MATURE SEGMENTS OF TÆNIA SAGINATA (Mosler and Peiper.).

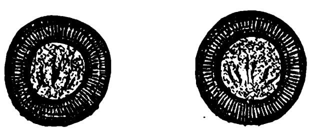


FIG. 94.—EGGS OF TÆNIA SAGINATA (Mosler and Peiper).

ments complete or the eggs from them escape in the feces. They are then taken up in the food, the covering of the egg digested and the embryos penetrate the tissues, ultimately lodging in the voluntary muscles and elsewhere. The em-

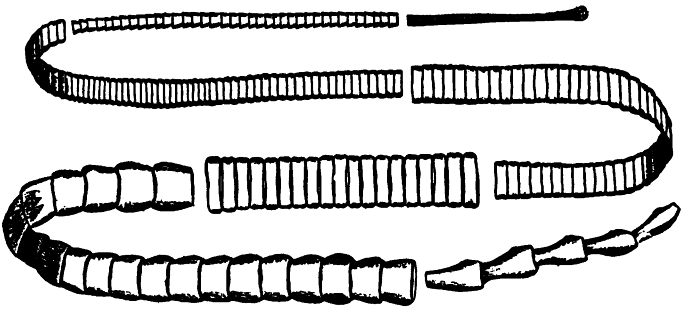


FIG. 95.—TÆNIA SAGINATA (Eichhorst).

bryo worm when lodged in the tissues is called a *scolex*, and is surrounded by a bladder-like body known as a *cysticercus*. When the animal food is eaten the embryos are set free, and attach themselves to the intestine.

FIG. 96.—HEAD OF DIBOTHRIOCEPHALUS LATUS (Blanchard).
a, a, Bothridies; *b,* neck.

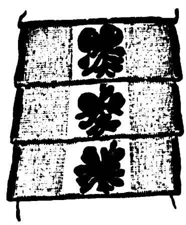


FIG. 97.—RIPE SEGMENTS OF DIBOTHRIOCEPHALUS LATUS (Mosler and Peiper).

Tænia solium, or pork tapeworm, is usually about 3 meters long. The head has a rostellum armed with a double row of from 26 to 30 hooklets and four suckers on the sides. The

uterus consists of a median tube with from 6 to 12 coarse lateral tubes. The genital pore is on alternate sides of the segments, which when mature are longer than they are broad.

The eggs are oval, about 30 to 35 microns in diameter, and consist of a peripheral striated zone and a central granular portion in which can be seen six lines representing hooklets. The embryos occur in pork as measles, and as cysticercus cellulosæ in the muscles, brain, and eye of man. They gain entrance in uncooked pork.

The **Tænia saginata** or **mediocanellata** is the beef tapeworm. Is quite common. It varies in length from 4 to 8 meters. Head is small, is flattened on the top, has no rostellum nor hooklets.

The uterus is like that of T. solium, but possesses from 20 to 30 lateral branches which frequently divide dichotomously. The genital pore is on alternate sides of the proglottides, which are longer than they are broad when fully matured. The eggs are a little larger and more oval than those of T. solium, otherwise very similar. Results from the eating of improperly cooked beef.

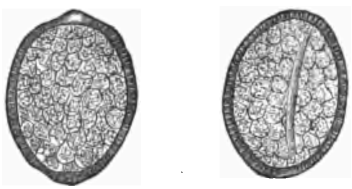


FIG. 98.—EGGS OF DIBOTHRIOCEPHALUS LATUS (Mosler and Peiper).

The **Dibothriocephalus latus** has for its host some kind of fish, usually the pike. It is the largest of the tapeworms, measuring from 5 to 9 meters in length and having at times as many as 4000 segments.

The head is long, flattened, and has two groove-like suckers on its sides. The neck is thin, gradually increasing in diameter.

The proglottides are broader than long and the uterus, instead of being branched, consists of a tube coiled upon itself in the center.

The genital pore is on the flat side of the segment, and always on the same side of the worm.

The eggs are oval and possess a shell-like cover which

has a hinged lid at one end. These eggs develop in fresh water into a freely moving, ciliated embryo that finally enters the digestive tract of the fish.

The **Tænia echinococcus** in its adult form is found in the intestinal tract of the dog, the larval form occurring in man and some of the lower animals.

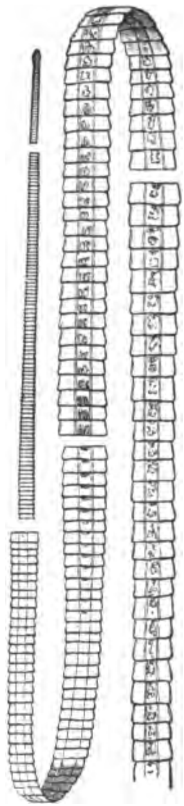


FIG. 99.—DIBOTHRIOCEPHALUS LATUS (Eichhorst).

It is quite short, about 4 or 5 mm. long, and consists of four segments. The head, which forms the first, is long, has four suckers and a rostellum having from 14 to 25 hooklets arranged in a double row.

The fourth segment is the largest and constitutes about two-thirds of the entire worm. It alone possesses a uterus which consists of a median portion with a few lateral branches. It contains numerous long oval eggs with very thin shells. The eggs enter the intestine, the shells are dissolved and the embryos set free. They penetrate various tissues, particularly the liver, become encapsulated, and slowly develop into cysts whose walls are made up of two layers—the outer cuticular and the inner granulo-cellular layer.

In the course of some weeks small projections grow from the inner layer and project into the primary cyst. These buds have hooklets and suckers and are embryo parasites.

This variety of cyst is the *echinococcus scoleciparius.*

In the *echinococcus hydatidosus* or *E. endogenes,* daughter and even grand-daughter cysts develop inside the original cyst. They probably result from a cystic change in the buds already

mentioned. Sometimes secondary cysts form on the outside of the wall, the *E. exogenes.*

The *echinococcus multilocularis* is the variety in which there are a great many small cysts surrounded by dense connective tissue. These cysts contain pigment and calcareous matter, but seldom scolices; are usually sterile.

These various forms of echinococcus cysts are filled with a clear fluid of about 1009 to 1015 specific gravity; is neutral or alkaline, contains no albumin, but sodium chlorid is present and sometimes sugar.

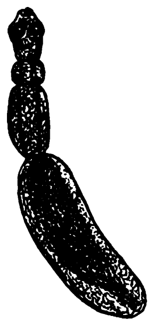


FIG. 100.—TÆNIA ECHINOCOCCUS; ENLARGED (Mosler and Peiper).

A cyst may become very large or the fluid disappear by absorption and inspissation.

It may be harmless or dangerous according to its location. May undergo suppuration.

Is usually found in the liver, but may occur in lungs, kidneys, spleen, omentum, and in the brain.

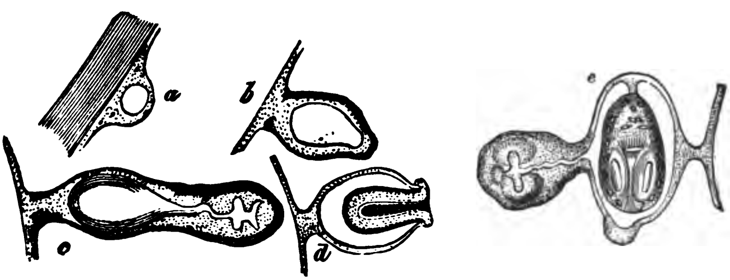


FIG. 101.—DEVELOPMENT OF OVUM. × 90 (Leuckart).
a, Suspended heads; *b*, primary rudiment of head; *c*, further development; *d*, intussusception of head; *e*, later budding.

The **Tænia nana,** or dwarf tapeworm, is from 2 to 3 mm. long. Its head is rounded, has four suckers and a rostellum that may be protruded or retracted, on which is a single

circle of from 22 to 27 hooklets. Are about 200 segments, all of which are broader than long.

The intermediate host is not definitely known; is thought to be some form of insect or snail.

The adult form alone is found in man. It attaches itself to the intestine by sinking its head deep into the mucous membrane.

The **Tænia cucumerina** or *elliptica* is the common tapeworm of cats and dogs. Is about 15 to 30 cm. long and has a head with a rostellum possessing 60 hooklets arranged in four rows. The rostellum can be protruded or retracted. The junction of the proglottides is much narrowed. Each segment has two genital pores, one on either side. The intermediary host is probably the dog louse or sometimes the flea.

Trematodes, or **sucking worms,** are flattened elliptic organisms that possess a sucking organ at the head end and another on the abdominal surface behind the short neck. They are usually hermaphroditic, but in some the two sexes occur.

The **Distoma hepaticum,** or liver fluke, is from 15 to 35 mm. long and 6 to 20 in width. Is pointed bluntly at each end and has two suckers, one at the head, the other on the ventral surface. Between the two suckers is the genital pore. The eggs are oval, 0.14 mm. in length, and provided with a lid at one end. Is hermaphroditic, the genital pore acting as a common opening for both sets of sexual organs. Multiplication takes place by the union of two parasites, each acting as both male and female. The adult parasite usually inhabits the bile-ducts of sheep, sometimes of man, in large numbers. It may obstruct the biliary ducts, giving rise to congestion and enlargement of the liver with later on degeneration and cystic formation. A water snail may be the intermediate host.

The **Distoma lanceolatum** is about 8 to 10 mm. long, 2 to 2.5 mm. wide. The anterior end is the more pointed. Has two suckers, quite widely separated, and in between them is the genital pore.

The eggs are oval, about 0.04 to 0.05 mm. long.

The snout has a spread-out membrane like an umbrella.

Is frequently found in combination with the D. hepaticum. Intermediate host unknown.

The **Distoma hematobium** has two distinct sexual forms, the male and the female.

The male is the larger, is from 12 to 14 mm. long and 1 mm. thick. The female is longer and thinner, 16 to 18 mm. long and 0.13 mm. thick.

The eggs are oval, 0.12 mm. long, and somewhat pointed at the ends.

In the act of fecundation the female crawls into a canal formed by the curving up of the sides of the male.

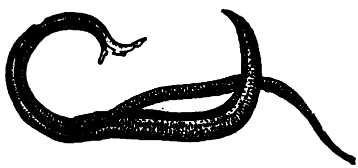


FIG. 102.—HUMAN BLOOD FLUKE (SCHISTOMA OR DISTOMA HÆMATOBIUM). × 5 (Leuckart).
The female is partially within the canalis gynæcophorus of the male.

These parasites occur in the portal, abdominal, and cystic veins. The eggs are produced in great numbers and obstruct and rupture the capillaries, thus escaping into the tissues. The wall of the bladder may become inflamed, ulceration take place, and eggs and blood escape in the urine.

The embryos are supposed to live in water and gain entrance by the alimentary tract.

The **Distoma pulmonale** is a form that has quite frequently been found in Japan and China.

Is 8 to 10 mm. long, 5 to 6 mm. wide. Resembles quite closely the liver fluke.

Is found in the lungs, usually near the periphery of a cavity. These cavities contain a muco-purulent liquid in which are found many eggs.

Nematodes, or **round worms,** are long round parasites, are not segmented, are provided with alimentary organs, and the sexes are separate.

The life-history, with the exception of the trichina, is completed within a single host.

The **Ascaris lumbricoides** is the commonest intestinal parasite in man. The female may be 40 cm. long and 5 to 6 mm. thick; the male 25 cm. long and 2 to 4 mm. thick. The body is brownish and has four longitudinal ridges extending the entire length. The head has three rounded lips, between which is the mouth.

The alimentary canal runs through the entire worm to an opening on the hinder abdominal surface.

The sexual organs occupy the posterior half of the body, the sexual opening being at the junction of its anterior and middle thirds. The uterus is double, thread-like, and twisted; may contain millions of eggs, which are from 0.05 to 0.06 mm. long, are oval, and are covered by a layer of clear albuminous matter which preserves them for a long time after being extruded.

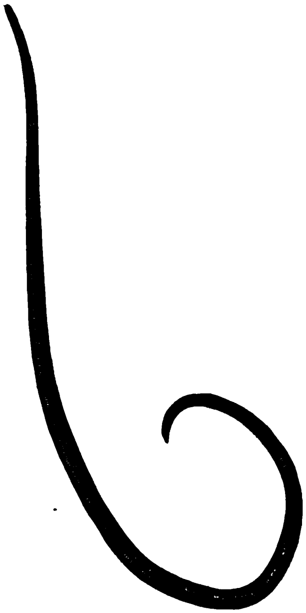


FIG. 103.—ASCARIS LUMBRICOIDES (FEMALE) (Mosler and Peiper).

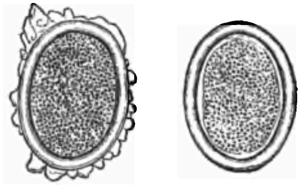


FIG. 104.—EGGS OF ASCARIS LUMBRICOIDES (Mosler and Peiper).

An intermediate host is not needed, the eggs developing in the human intestine. They may occur singly or in numbers. Are found in the small intestine, but may migrate, en-

tering the gall-ducts, the stomach, the esophagus, and even the larynx or nasal cavities.

May obstruct the intestine, or set up inflammation with perforation and abscess formation. Also cause obscure nervous symptoms.

The **Oxyuris vermicularis,** *Thread* or *Seat worm,* is commonly found in children.

Is white in color; the female is from 10 to 12 mm., the male 2.5 to 5 mm. long. The tail of the female is long and tapering, that of the male blunt and curved upon itself. The mouth lies between three lips. The genital pore is anterior in the female, posterior in the male. The eggs are oval, about 0.005 mm. long, and contain embryos with sharp posterior ends.

FIG. 105.—OXYURIS VERMICULARIS AND EGG (after Heller).
a, Natural size; *b,* egg.

The parasites live in the large intestine, usually in great numbers. May leave the rectum and enter the vagina and urethra in girls, causing much irritation and itching. The eggs are swallowed, hatch in the upper intestine, and the female worms becoming fecundated form more eggs.

The **Eustrongylus gigas** is a large round worm found in the pelvis of the kidney or ureter, usually in horses or cattle, but sometimes in man. The female is about one meter long and 8 to 12 mm. thick, the male about one-third as long. Is reddish in color, the anterior end is retracted, and around the mouth are six papillæ. In the male the posterior end is expanded, and a spicule projects from the cloaca.

The **Filaria medinensis,** or "Guinea-worm," is a very slender round worm about one meter long. The female only is certainly known. It has a circular oral opening with four hooklets. The tail is sharply pointed.

The greater part of the worm consists of a uterus which contains enormous numbers of embryos. These escape, especially when water is brought in contact with the ulcer from

which the worm extrudes. The embryos live in the water, and one view is that a minute crustacean is the intermediate host.

This worm is found in the tropics and occurs in the subcutaneous tissues, particularly of the feet and hands.

The **Filaria sanguinis hominis** as commonly found is the embryo of a worm that is rarely seen in the adult form. The usual form is the *Filaria nocturna.* The adult is from 8 to 10 cm. long and lives in the larger lymphatic vessels. No eggs are laid, but great numbers of living embryos are set free in the lymphatics and thence into the blood. The embryos are about 0.25 mm. in length and the diameter a little greater than that of an erythrocyte. The head is broad and blunt, the tail tapering. They appear in the blood only during

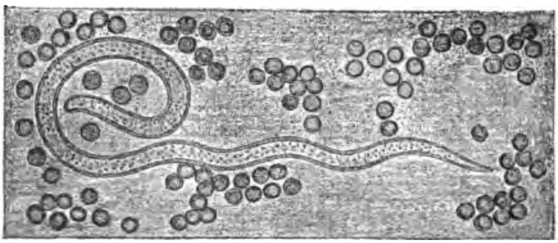


FIG. 106.—FILARIA EMBRYO, ALIVE IN THE BLOOD (F. P. Henry).

the period of rest. If the person works at night and sleeps during the day, they will be found during the latter period.

They escape through the kidneys into the urine in attacks of hematuria.

The mature worm, from obstruction to the lymphatics, may give rise to marked enlargements, such as lymph-scrotum and elephantiasis.

The *Filaria perstans* is a form that is found in the blood at all times, day or night. The embryo alone is known. The *Filaria diurna* occurs in the daytime only.

Filariasis is common in Egypt, India, and Africa, and the intermediate host is a mosquito, one of the Culex variety.

The **Uncinaria (Anchylostoma) duodenalis** is a small

round worm found in the upper intestine of man. The male is from 7 to 11 mm. long and 0.46 mm. wide, the female from 7 to 16 mm. long and 0.63 mm. broad. The head of the worm is cylindric and bends backward. The mouth has three pairs of sharp incurved hooklets and opens directly into an esophagus that occupies the anterior third of the worm.

The posterior end of the female is pointed and has two openings, the excretory and the genital pore. The tail of

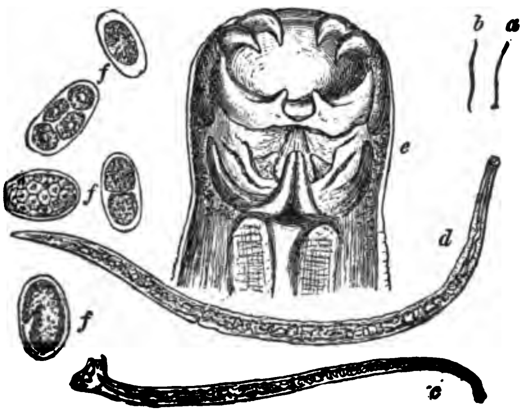


FIG. 107.—UNCINARIA DUODENALIS (von Jaksch).
a, Male, natural size; *b*, female, natural size; *c*, male, magnified; *d*, female, magnified; *e*, head, greatly magnified; *f*, *f*, *f*, eggs.

the male is expanded and is arranged like a three-leaved cup.

The eggs appear in the feces as oval, thin-shelled, and doubly contoured bodies about 0.36 to 0.63 mm. long. The number of eggs is enormous. Has been estimated that more than four millions may occur in a single stool. After exposure to the air the embryos escape from the eggs in about six days and continue their existence in the water. They may gain entrance by means of drinking-water or, as has been shown, the embryos may penetrate the skin of the feet.

The adult worm may occur in small or large numbers. It attaches itself to the wall of the intestine and sucks the blood for its nourishment. If the worm lets go, there remains an area of ecchymosis with a small point of hemorrhage in the center. It is thought that the parasite may inject into the wound some substance that interferes with the coagulation of the blood.

FIG. 108.—TRICHOCEPHALUS DISPAR (Heller).

a, Female; *b*, male (natural size).

If the organisms occur in great numbers, the loss of blood may be so severe as to cause a very marked anemia.

This condition exists in Egypt, southern Europe, and Brazil.

The **Uncinaria americana** is a closely related worm that is widely distributed in America, particularly in the sandy soil of the Southern States. It has a much smaller head, smaller and blunter teeth, and is less dangerous than the European variety.

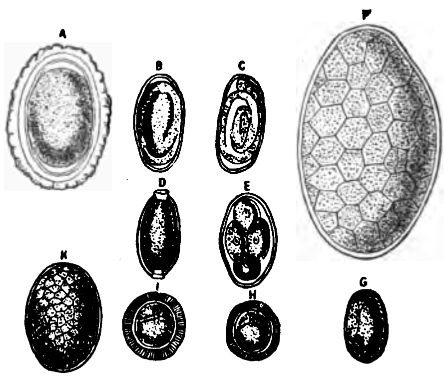


FIG. 109.—EGGS OF VARIOUS WORMS FOUND IN THE ALIMENTARY CANAL OF MAN. × 400 (Mitchell).

A, Ascaris lumbricoides; B, C, Oxyuris vermicularis; D, Trichocephalus dispar; E, Uncinaria duodenale; F, Fasciola hepatica; G, Dicrocœlium lanceolatum; H. Tænia solium; I, Tænia saginata; K, Dibothriocephalus latus.

The **Anguillula intestinalis** is a very motile worm, about 2 mm. long, and very thin. Is found in the intestine. The embryos were thought to be a different form of parasite and were formerly called *A. stercoralis*. Occurs in China and is found in some cases of diarrhea.

The **Trichocephalus dispar,** or "whip-worm," is found in the large intestine of man, but is of little pathologic importance.

Is from 4 to 5 cm. long and is peculiar in that the anterior two-thirds are very slender, while the posterior third is thicker. In the male the posterior portion is spirally coiled, in the female is slightly curved.

Fig. 110.—Fresh Muscle Trichinæ (Mosler and Peiper).

The eggs are about 0.55 mm. long and at each end have a button-like excrescence.

The **Trichina spiralis** is a very important parasite that undergoes development in two hosts.

It occurs in two forms in man and the lower animals, as an intestinal fully developed worm and as an encapsulated embryo in the muscular tissue. Is most common in hogs. The adult female is from 2 to 4 mm., the male 1.5 mm. in length. The eggs develop into embryos while within the mother. When an encysted embryo is taken into the stomach the gastric juices dissolve the shell, and the parasite is set free. It very rapidly matures, and in the course of from five to seven days eggs are discharged. Within a few days a couple of thousand embryos will have been liberated. These young parasites penetrate the walls of the intestine, gain entrance either into the blood or the lymphatics, most probably the blood, and in the course of about ten days become lodged in the voluntary muscles.

In the muscle fibers the embryos become encysted in two

to three weeks. There is a deposit of lime salts around the curled-up embryos which may either die and become calcified or remain alive for years. The encysted form appears as a small white point.

Infection in man takes place by the eating of meat (measly pork) that contains the trichinæ and that has not been properly cooked. A temperature of 65° C. kills the parasite, but pickling and smoking destroy those only which are in the superficial parts, those deep within being unaffected.

When the embryos escape from the cysts into the intestine severe vomiting and diarrhea may occur. During the emigration to the muscles the symptoms are those of muscular rheumatism. In this disease there has frequently been noticed a very great increase of the eosinophile cells in the blood.

ARACHNOIDEA

The insects are external parasites which may prove dangerous by means of their own metabolic products, by acting the part of intermediate host for some parasite, or by mechanically carrying the source of infection.

The first class is not very important. In the second is the mosquito, which may in some of its varieties transmit malaria, yellow fever, or filaria sanguinis hominis.

Flies may mechanically convey typhoid bacilli from feces to articles of food.

CHAPTER XV

POST-MORTEM EXAMINATION

The purpose primarily of post-mortems is to determine the cause of death. Frequently there are found several diseased organs. The question then arises as to the order in which they were involved and from what their condition resulted.

The examination may be divided into the inspection of the external appearances and into the examination, both macroscopic and microscopic, of the internal organs.

During the post-mortem there should be some one to take notes on the various findings. If possible, the clinical history of the case should be learned before the autopsy is begun.

EXTERNAL INSPECTION

The appearances should be carefully noticed, as they are of great importance, particularly in medico-legal cases, such as approximate age; sex; height, measured as the body lies on its back between two uprights; bodily development; condition of nutrition; general condition of the skin; amount of fat present.

Distinguishing marks; irregularities of the teeth, deformities of any kind; fractures; wounds, whether ante-mortem or post-mortem. If the former, there may be indications of bleeding, edges will gape, and there will be some signs of inflammation or beginning repair. If post-mortem injury, there will be no escape of blood into the tissues, no bleeding on incision, no inflammation or repair.

Presence of edema, most common in the lower extremities at the ankles, the scrotum, and labia.

Signs of decomposition, first appearing as a greenish dis-

coloration of the abdomen and prominence of the superficial veins due to the staining of the tissues by blood-pigment from degenerated erythrocytes.

Rigor mortis, its degree and extent; post-mortem lividity, or hypostases, is present in dependent parts and disappears on pressure; diffuse pigmentation, the result of decomposition, does not disappear on pressure.

The condition of the pupils, whether dilated, contracted or unequal; the sclera; size and shape of thorax; distention or retraction of abdomen.

INTERNAL INSPECTION

The generally accepted order of examination is brain, spinal cord, thorax, and abdomen. The brain should be examined first, so that the amount of blood in the cerebral vessels can be determined. As in this country autopsies are usually limited to the thorax and abdomen, they will be first described.

The autopsy should not be done by artificial light, as the color values are distorted.

The operator should stand on the right side of the body and should grasp the handle of the knife as he would in cutting bread. The knife should be drawn and not pressed or shoved into the tissues. The main movement should come from the shoulder, the secondary from the elbow-joint.

Incisions into organs should be deep and single rather than shallow and numerous, as a broad surface gives much more information than a narrow one.

The primary incision is a long single one extending from the larynx along the median line to the pubes, passing to the left of the umbilicus so as to avoid the round ligament of the liver. The knife should be held almost horizontal so that the belly and not the point is used.

Over the sternum the incision extends to the bone; over the abdomen it should go only as deep as the subcutaneous tissue or the muscle. The abdominal cavity is opened by making a small incision through the peritoneum a little below the xiphoid cartilage. Two fingers of the left hand are in-

serted, the flaps drawn upward, and the incision continued between them down to the pubes. The recti muscles may be divided just above the pubes, care being taken not to cut the skin.

The abdominal flaps in turn are seized with the left hand and strongly drawn outward. This renders the tissues tense and they are dissected away from the ribs by long sweeping cuts. The operation begins over the lower border of the ribs and is carried up a little above the articulation of the clavicle and outward as far as the anterior axillary line.

The abdomen should then be inspected, first without touching anything. The organs and their relations should be noted; the character and the amount of any fluid present and any that runs off should be caught and measured. The omentum should be removed and the intestines examined, also the appendix and the mesenteric lymph-nodes. The peritoneum normally is smooth, glistening, and transparent, the same as any serous membrane.

The height of the diaphragm is determined by introducing the hand under the costal margin and finding at what rib or interspace it reaches in the mid-clavicular line. On the right side is usually about the level of the fourth rib or interspace, on the left is about the third rib or interspace. If lower than normal it generally indicates fluid in the pleural cavity, enlargement of the thoracic organ or new growths.

Before opening the thoracic cavity, if pneumothorax be suspected raise the skin flap and fill the pocket thus formed with water. Puncture below the level of the water and watch for bubbles to come through.

The thorax is opened by cutting through the costal cartilages, from the second down, by holding the knife almost horizontal and resting it on the rib in advance before the previous one is completely severed. The division should take place at the junction of the rib and cartilage. Instead of using a knife the intercostal spaces may be first opened and the ribs then divided by means of the costotome. By this method there is less danger of cutting into the lungs.

The sternum is elevated by grasping the xiphoid cartilage;

the attachment of the diaphragm is divided on either side. It is freed from the underlying tissues by long cuts of the knife, which should be made close to the bone so as to avoid the pericardium. When the first rib is reached its cartilage is divided about 2 cm. further out than that of the second. The edge of the knife should be directed upward and outward, the handle being beneath the elevated sternum.

The clavicle may be disarticulated by cutting from below along the irregular line of the sterno-clavicular articulation. By this method there is less danger of wounding the large vessels at the base of the neck, a very important point in medico-legal cases. The articulation may be divided from above by entering a narrow knife along the line of the joint, which curves down and out. The handle of the knife should incline so that it is nearer the cadaver's chin than is the blade. If held perpendicular both the clavicle and sternum interfere, as the joint slants. If properly carried out, it can be done without any great force being exerted, short up and down strokes being used. The sternum should then be twisted out rather than cut, otherwise the large vessels of the neck may be divided.

If the cartilages have become calcified, care should be taken not to cut one's hands on the exposed ends. Protection can be had by drawing the dissected flap of skin over the edges.

If removal of the sternum is not allowed, the thoracic organs may be removed from below by separating the diaphragm from the ribs.

On removal of the sternum, the lungs and the pericardial sac are exposed. One should notice how near the lungs come to meeting in the median line. Ordinarily they will touch at the level of the second rib.

The pleural cavities should be examined. One should determine the presence or absence of fluid, its character and amount. Adhesions should be looked for, and the amount of force required to break through them is a guide as to their duration. If the adhesions are very dense, the best way when one comes to remove the lungs is to strip off the costal layer of the pleura with the viscera.

In opening the pericardium the sac is picked up by the fingers and an incision made upward to where the large vessels enter at the base of the heart. This cut is continued downward to the lower right border. From the middle of this incision one is made down to the apex. The cut should be made from within out, so as to avoid wounding the heart.

By lifting up the apex of the heart the amount and character of the contained fluid can be determined. Is usually only 5 to 10 c.c.

The presence or absence of adhesions between the heart and pericardium should be noted. Sometimes the entire cavity may be obliterated.

Before making any incisions into the heart, its size, shape, and position should be noted. The distention or contraction of the various cavities should be determined.

Opening of the Heart.—This may be done either *in situ* or after removal from the body. As a general thing, it is best to remove the heart before making any incisions. It is then easier to make the openings, but there is more danger of bacterial contamination occurring.

To remove the heart one grasps the apex with the left hand and lifts up the entire organ. By three or four long cuts made from below upward, first severing the inferior vena cava, then the left pulmonary vein, and finally the remaining vessels, the heart is removed. Care should be taken to wound neither the auricles nor the underlying esophagus.

In opening the heart the primary incisions are made with a knife and then united by using long straight scissors with blunt points or else a cardiotome.

The heart is then placed in a position corresponding to its normal one within the body; the apex directed toward the operator, the anterior surface being upward. The cavities are then opened in the order in which they receive the blood.

The *right auricle* is opened by making an incision from the inferior to the superior vena cava and then continued into the auricular appendage.

In opening the *right ventricle* the first cut extends through the tricuspid valve down to the end of the cavity. The sec-

ond incision is made about the middle of the primary one and at almost right angles to it. This cut should be high enough up to avoid cutting through the insertion of the anterior papillary muscle. It is continued through the pulmonary valve, following along a slightly marked ridge of fat; by so doing the orifice is opened between the left anterior and the posterior leaflets.

The *left auricle* is opened by uniting the four pulmonary veins and continuing into the auricular appendage.

The *left ventricle* has the first incision made through the mitral valve between the two papillary muscles along the left border of the heart to the apex. The second incision is made by beginning at the apex at the end of the first and continuing upward close by the interventricular septum and parallel to the anterior coronary artery. The upper end of the cut should pass about midway between the pulmonary orifice and the left auricular appendage. An aortic leaflet is generally divided in so doing.

As the auricles are opened the clots should be removed and the valves carefully examined. The size of the opening should be noted, so as to determine whether or not stenosis or dilatation exists. The test of valvular competency by filling the cavity with water is unreliable.

The ventricles are freed from blood and their valves examined.

The anterior coronary artery is examined by opening with a pair of probe-pointed scissors. The posterior coronary is best seen by placing the tip of the left forefinger over the orifice of the vessel in the aorta, then cutting from without toward the finger-tip until the artery is reached. By so doing the aorta is not injured.

The heart should be weighed, its walls measured, the condition of the valves and muscle noted, and the aorta above the valves examined for atheroma.

Lungs.—In removing the lung all adhesions should be broken up or cut through. It is then drawn forward and downward, the root being grasped from above between the fingers of the left hand. The primary bronchus is divided

behind the left hand and the lung is lifted upward, the remaining attachments being divided.

If there are dense adhesions between the lung and the diaphragm, it is best to remove the latter with the lung by cutting through the attachments to the ribs. Be careful to avoid wounding either esophagus or aorta.

The two organs can be distinguished from each other by remembering that the anterior edge is thin while the posterior is rounded and the bronchi are on the inner surface. Also that the right lung has usually three lobes, the left two only, although variations occur.

The lungs may be opened by either a long incision extending from apex to base or by a horizontal incision taking in the entire width of the organ. The bronchi and blood-vessels should be opened with small scissors.

The cut surfaces should be carefully examined, the color, amount of blood, presence of fluid, solidity, degree of crepitation, smoothness, and friability noted. Portions of the more solid areas should be placed in water to see if they will float.

More room for the examination of the abdominal organs can be gained by cutting through the diaphragm on either side of the liver and turning that viscus upward.

The **spleen** is removed by drawing it gently toward the mid-line and the vessels cut close to the hilum. If adherent to the diaphragm, care should be taken that its capsule is not torn.

Its size, shape, and density should be noted, as well as the appearance of the capsule, trabeculæ, blood-vessels, lymph-follicles and pulp.

Intestines.—The intestines are removed next. The omentum may either be removed when the abdominal cavity is inspected or left till later. It is freed from the transverse colon by dividing it close to the gut with a knife.

The most convenient way to dispose of the intestines is by freeing the sigmoid flexure from the mesocolon and dividing just above the rectum. The transverse colon is freed by dividing the two folds of the lesser omentum, the ascending by dividing the mesocolon.

To remove the small intestine it should be grasped with the left hand and sufficient force exerted to keep the mesentery in a state of tension. The blade of the knife is held parallel to the intestine and the mesentery is cut at its attachment by means of to-and-fro motions. As the intestines are set free they should be received into a pan. When the duodenum is reached it is ligated and cut on the distal side. The mesentery is then removed. The gut is then opened, the large intestine along one of its longitudinal muscular bands, the small along its mesenteric attachment, as opposite to that side the most important lesions involving the lymph-nodes and Peyer's patches are found.

In order to determine whether or not there is any obstruction of the hepatic or common bile-ducts the duodenum should be opened *in situ*. The incision should be along the anterior wall and extend from the pylorus to where the duodenum passes beneath the mesentery. The opening of the bile-duct is usually marked by a small papilla. Pressure is first made on the common duct, and the opening watched to see if any obstruction prevents the escape of bile. Pressure should then be made upon the gall-bladder to see if its contents can escape.

The **kidneys** may be removed along with the adrenals by making an incision to the inner side and then above the adrenal, then cutting along the outer convex border of the kidney through the peritoneum and the perirenal fat. The kidney is shelled out by using the left hand and the vessels are cut from above downward and as near to the aorta as possible. When they are divided the organ is raised and the tissues loosened with the fingers until the ureter is disclosed, when it is severed.

When the entire urinary apparatus is diseased all the organs may be removed together by first dissecting the ureters till the bladder is reached, then turning the kidneys downward, after which the pelvic organs can be taken out.

Sometimes the kidneys may be removed without the adrenals, in which case the latter are either opened *in situ* or

removed separately. The right adrenal is attached to the under surface of the liver and must be dissected free.

The left kidney is generally removed first.

In examining the kidney it is held between the thumb and fingers with the convex surface upward. A deep longitudinal incision is then made down to the hilum. The capsule can then be stripped by getting hold of it with the thumbnail.

The size, color, condition of the surface, and density should be noted. Portions of the kidney substance may be removed with the capsule. The presence of cysts or of infarcts should be determined. On section the relative proportion between cortex and medulla, the color of the cut surface, the presence of abnormal substances, amount of connective tissue, the normal markings of the kidney, the blood-vessels, glomeruli, the tubules of the cortex and of the medulla should be carefully noted. The pelvic mucous membrane should also be examined.

The **liver** is removed by raising up the right lobe and freeing it from all attachments, then the left lobe. If adherent to the diaphragm, remove it with the liver. The portal vein and the common bile-duct should be examined.

The tissue is exposed by one or more long cuts on the anterior surface across both lobes. Should note the amount of congestion, the degree of fatty changes, the amount of connective tissue present, and the degree of bile staining.

In removing the **stomach** a portion of the duodenum is cut through and lifted up and the stomach, together with the pancreas, freed by incisions from below upward. The stomach is dissected free from the pancreas and opened along its greater curvature. If any marked lesions are noticed from the outside, the incision should be so made as not to damage them.

The **pancreas** is examined by making numerous transverse incisions. Should be on the lookout for fat necrosis. The duct may be slit open along its course.

In removing the **organs of the neck** it is best, if allowed, to continue the skin incision up to the symphysis of the jaw.

The skin is dissected free as far as the hyoid bone and upward to the chin. The tissues are loosened by passing the knife around inside the clavicles. The head should be allowed to drop back and a long thin knife is inserted at the symphysis beneath the tip of the tongue. By means of a sawing motion the muscles are divided first on one side and then on the other as far as the vertebral column. The esophagus and the trachea are lifted up and the dissection continued till the posterior wall of the pharynx is divided. The tongue is drawn downward and an incision made on either side, well out, so as to divide the lateral pillars of the fauces without wounding the tonsils. The soft palate is separated and the structures removed.

The esophagus is opened by being cut along its median line posteriorly from the pharynx down. It is then pulled to one side, when the larynx and trachea are divided along the posterior wall.

The lobes of the thyroid gland should be cut in their long diameters.

The **pelvic organs** are removed by dividing the peritoneum along the brim of the pelvis and dissecting it with the fingers till the posterior surface of the rectum is freed. The cut end of the rectum is drawn upward and toward the pubes while the attachments posteriorly are dissected away. The pelvic organs are now attached only at the external openings. These are divided anteriorly close to the pubes and posteriorly along the outlet of the pelvis.

The **rectum** is opened along its posterior wall and cleaned.

In opening the **bladder** a slight incision is made in the anterior wall of the fundus and with a pair of scissors the cut is continued along the anterior wall through the urethra.

The **uterus** is opened by making an incision along the anterior wall from the fundus to the cervix. Two secondary incisions extend from the upper end of the first cut to the openings of the Fallopian tubes. The *vagina* is opened by carrying the incision downward. It should be done from this direction so that the operator may be sure that any foreign substance found in the uterus was not conveyed there

on the point of his scissors, an important consideration in medico-legal cases. The ovaries are opened along their greatest diameter.

The **testicles** can be drawn up through the internal ring and examined without any injury to the scrotum. The greater portion of the penis can be removed by incising the skin as far as the middle of the dorsum and dividing just behind the corona. Is then dissected free and withdrawn underneath the arch of the pubes.

The structures now left for examination are the inferior vena cava, the thoracic and abdominal aorta, the iliacs, and the thoracic duct. They should be slit open.

Removal of the Brain.—To displace the scalp an incision is carried over the vertex from the tip of one mastoid process to the tip of the other. This should be made from within outward, as by so doing the hair will be divided but not cut. The periosteum should be cut through and the two flaps dissected free. The anterior one extending nearly to the orbits, the posterior is carried backward to the occipital protuberance.

The temporal muscle should be left, but is divided at the point where the cut of the saw is to be made.

The line of opening the skull extends from a point just behind and above the ear, forward over the frontal eminences to a corresponding point on the opposite side. By carrying this line posteriorly over the occipital protuberance the path of the incision is marked out. The incision is started over the forehead and carried backward over the line mapped out. By bracing the saw with the thumb of the left hand and drawing backward a correct start can be made. Continue the ncision, first on one side and then on the other, till the mastoid processes have been reached. Care should be taken not to injure the dura. Is often best not to cut through the inner plate of the skull but to break it with a chisel. A posterior incision is continued backward a little above the occipital protuberance.

It should be noted that there are four points where the skull is particularly thick and two where it is very thin. The

thick points are over the mastoid processes and in the median line anteriorly and posteriorly. The thin points are over the temporal fossæ, where the skull is so thin that a few blows with a chisel will complete the separation.

By inserting the end of a chisel in the mid-line anteriorly and then twisting it the calvarium will be loosened sufficiently to allow the inserting of a hook. By pulling, the skull-cap will be freed unless there are dense adhesions between it and the dura. It is sometimes necessary to remove the calvarium together with the dura.

To remove the dura insert a small knife and cut from within outward along the line of the saw incision. Reflect the two flaps along the mid-line and examine the surface of the brain. The convolutions should be round and not flat. The dura is freed from its attachment to the crista galli and dissected backward. It is separated from the pacchionian bodies, to which it is adherent, by means of slight cuts. The membrane should be examined carefully and the longitudinal sinus opened. The dura should not be cut through posteriorly but should hang down.

The pia is now exposed and the external appearances of the brain should be noted; the degree of congestion, the presence of edema, of tubercles, purulent collections and local or general thickening.

The brain is removed by gently elevating the frontal lobes until the optic nerves are seen. Care should be taken not to cut the olfactory nerves. The optic nerves are cut as far forward as possible, then the carotids are severed.

The tentorium is cut by a sawing motion close to its attachment to the petrous portion of the temporal bone. The various cranial nerves are then divided.

The spinal cord is severed by inserting the scalpel as far as possible into the spinal canal and cutting through with an oblique incision from one side to the other. At the same time the vertebral arteries are cut.

The brain during this should be supported by the left hand.

The base of the skull should be examined, and if a fracture is suspected the dura is stripped off.

To examine the brain place it on its vertex with cerebellum toward one. The pia and the cranial nerves should be examined. Then carefully note the arteries for changes in size, malformations, presence of atheroma, aneurysms, or of tubercles. Separate the Sylvian fissure and examine the vessels there as tubercles, emboli, aneurysms, and hemorrhage may be discovered although absent elsewhere.

To section the brain the following method is generally employed: The brain is placed on its base and the hemispheres separated till the corpus callosum is exposed. The first incision is made into the lateral ventricle about 3 mm. from the median line of the corpus callosum and extending into the anterior and posterior cornua. Posteriorly the convolutions over the cornua are cut through. A series of incisions are made through the hemisphere just external to the basal ganglia with their edges coinciding but going at an angle of about 45 degrees. This gives a number of wedge-shaped portions, held together by the pia, which should not have been removed.

The brain is turned half around and the process repeated on the other side. Care must be taken not to injure the ganglia when opening the ventricle.

The corpus callosum is gently lifted and divided by passing a knife through the foramen of Monro and cutting from below upward. The cut portions are reflected, exposing the velum interpositum and the choroid plexus. The third ventricle is disclosed by drawing back the velum interpositum.

The vermiform process is cut through, opening the fourth ventricle; the aqueduct is cut and all the ventricles are exposed.

The corpora quadrigemina are found by dividing the right posterior pillar of the fornix and reflecting it to the left.

The basal ganglia are exposed by making a series of transverse cuts, the brain being supported from below by the left hand.

The pons and medulla are cut transversely into thin sections.

The cerebellum is divided along the median line into two halves, each of which is subdivided by a series of incisions at right angles to the primary cut.

This method is the one that is employed when the organ has to be examined when fresh. In this way, however, the relations of the different parts may be much disturbed. The best way is to harden the entire brain, either in Müller's fluid or in formaldehyde. When hardened a series of incisions is made transversely through the entire thickness of the organ and extending from one end to the other.

In cutting into the fresh brain the blade of the knife should always be wet so as to prevent its adhering. As long as the pia has not been divided the brain can be restored to its normal form by replacing the wedge-shaped pieces.

The middle ear and the orbits are exposed by breaking through the roof. In removing the eye the anterior half should be left and the space filled with cotton. The incision is made just posterior to the conjunctival margin and the optic nerve should be removed with it.

Removal of the Spinal Cord.—This may be done either before or after the abdominal and thoracic cavities have been examined.

The body is placed prone with the head over the edge of the table and a block under the abdomen so as to lessen the lumbar curve. An incision is made from the occiput to the sacrum along the spinous processes. The skin and muscles are dissected away on either side, exposing the laminæ at the bottom of the groove, which should be thoroughly clean. By means of a double- or single-bladed saw the laminæ should be divided so as to enter the spinal canal at its outside limits. The laminæ of the cervical vertebræ are more easily bitten through with strong bone forceps.

Divide the spinous processes on either side, cut the ligaments in the lower lumbar region, and lift them up to the neck.

The dura over the cauda equina is picked up with forceps and the nerves are cut from below upward; if done carefully, the posterior root ganglia can be removed with the cord. At no time should the cord be pulled or bent.

The dura should be opened by a longitudinal incision, made with probe-pointed scissors, either along its anterior

or posterior surface. Transverse sections of the cord, about 2 cm. in thickness, should be made; the incisions coming in between each two pair of nerves and leaving the segments attached to the pia.

A diagnosis is frequently made with difficulty from the fresh macroscopic appearance of the cord.

CHAPTER XVI

LABORATORY TECHNIQUE

EXAMINATION OF FRESH MATERIAL

The examination of fresh material may be made by teasing the tissue in water or preferably 0.6 per cent. saline solution. This, however, may not be satisfactory unless the tissue has been allowed to remain in some fluid long enough for the cells to become separated from the basement membrane. This is known as *maceration;* the following fluids are used for this purpose.

1. Thirty-three per cent. alcohol (Ranvier), in which soak the specimen twenty-four hours.

2. Very weak chromic acid solutions, 1 : 10,000, or its salts. Müller's fluid is especially useful for nervous tissue. Leave in the acid twenty-four hours; in the latter three to five days.

3. One per cent. osmic acid for twelve to twenty-four hours. Is useful if there is any fat present.

4. Potassium hydrate, 33 per cent., for from fifteen to twenty minutes. The specimen should be examined in the same fluid, as water distorts the cells. To preserve the tissue wash in 50 per cent. acetic acid, then in water, and after staining in alum carmin can be mounted in glycerin. Is good for the examination of tissues or tumors that contain smooth, involuntary muscle-fibers.

5. Arnold's method: The small pieces of tissue are placed for five to ten minutes in 1 per cent. acetic acid, then for twenty-four to forty-eight hours in the weak chromic acid solution. They may finally be stained with picrocarmin.

Various reagents may be used in the examination of fresh specimens to render them transparent, to bring out certain details, or to cause various substances to disappear.

1. Glycerin clears the tissues and has the advantage of not changing chemically nor getting thin. Permanent mounts may be made by sealing the edges of the cover-glass with paraffin.

2. Potassium acetate in a saturated watery (50 per cent.) solution has a clearing action similar to but less marked than glycerin.

3. Acetic acid: Has the advantage that it causes the nucleus to shrink and the connective tissue to swell and become transparent. It does not affect fat, but dissolves the proteid granules, so differentiates the two processes. Elastic fibers and micro-organisms are unaffected, so stand out prominently against the changed connective tissue. The acid may also be used to dissolve calcium salts. Solutions of 1 to 2 per cent. are generally employed, but the pure glacial acetic acid may be used.

A solution of acetic acid with fuchsin may be employed and in that way stain the nuclei.

4. Weak watery solutions of iodin. The following solution (Lugol's) is mixed with 3 to 5 parts of water:

Iodin	1.0
Potassium iodid	1.0
Distilled water	100.0

This brings the nucleus and the cell contour more plainly to view and also stains glycogen and amyloid particles brown.

5. Potassium and sodium hydrate solutions of from 1 to 3 per cent. have the power to dissolve most tissues, but do not affect elastic tissue, fat, bone, pigment, bacteria, or amyloid. Thirty-three per cent. solutions dissolve the cement substance and isolate the cells. This reaction takes place in a few minutes.

6. Osmic acid in 1 per cent. watery solution will stain fat, black or brown.

7. Hydrochloric acid in from 3 to 5 per cent. is used for the recognition of lime salts, either in bone or in the tissues which it dissolves with the production of bubbles of CO_2.

8. Fresh preparations may be stained by allowing a few drops of watery stains to pass under the cover-glass and then washing out the excess. Methyl-green, Loeffler's methylene-blue or acetic acid fuchsin may be used. Hematoxylin is unsuitable.

FIXATION AND HARDENING

If a more exact examination is desired, the tissues must be hardened and fixed. The material should be placed in the fluid used as soon as possible after it has been obtained. The point desired is that the conditions as they exist in the tissues during life shall be retained.

The different solutions vary greatly in their power of penetration and also in their effects upon different tissues. The action is facilitated by cutting the specimen in small pieces. After fixing and hardening it is generally necessary to thoroughly wash so as to remove all traces of the agent employed.

The points to be observed are:

The specimens should not be more than 2 cm. in thickness.

The volume of reagent used should be from ten to fifteen times larger than the bulk of the specimen.

Place a layer of absorbent cotton or filter-paper in the bottom of the jar so that the tissue may be acted upon by the fluid from all sides.

After sufficient hardening remove the specimen and wash it in running water for twelve to twenty-four hours. It is then passed through alcohols of various strengths—70, 80, and 90 per cent., about twenty-four hours in each.

Alcohol.—It is used for rapid work and particularly if bacteria are suspected. It is not good for nervous tissue. Specimens should, as a rule, be put in weaker alcohol before being placed in absolute. This method is not used as much as formerly on account of the shrinking and distortion of the tissues and the destruction of the red blood-corpuscles.

The so-called absolute alcohol is usually little more than 95 per cent. To extract the water, copper sulphate should

be heated till the blue color disappears and then added to the alcohol. The alcohol should be filtered before using and the copper sulphate reheated when it begins to turn blue.

Formalin.—This reagent is being used very greatly in place of alcohol. It has numerous advantages. The hardening takes place rapidly, the erythrocytes and other pigments retain their natural colors.

As formalin is bought it consists of a 40 per cent. solution of formaldehyde in water. The strength commonly used is a 1 : 10 or a 4 per cent. solution.

The tissues are left from four to six hours in the 4 per cent. solution, then thoroughly washed in water, and finally passed through alcoholic solutions of varying strengths.

Formalin is also used in combination with other mixtures, particularly as Orth's solution. This is made by adding ten parts of formalin to one hundred parts of Müller's fluid. This should be made fresh, as in the course of five or six days there is a crystalline precipitate formed. This fixes nuclear figures very well and hardens small pieces of tissue in from three to six hours. It is particularly important that they should be very carefully washed in running water. Is good for nervous tissues.

3. **Mueller's fluid** is made up of:

Potassium bichromate................	2.5
Sodium sulphate.....................	1.0
Distilled water.....................	100.0

This should be used in large quantities and should be changed every second day for about five times and then be replaced whenever the solution becomes cloudy. To prevent the growth of mold one gram of bichlorid of mercury should be added to two liters of the fluid.

For thorough hardening of small objects from ten to twelve weeks is required; for a large object like the brain, a year. The process can be hastened by placing the preparation in an incubator and frequently changing the fluid.

After complete hardening the preparation is carefully washed in water, and then run through increasing strengths

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of alcohol. The sections stain well with hematoxylin and eosin. The red corpuscles are well preserved.

4. **Erlicki's fluid** consists of:

Potassium bichromate	2.5
Sulphate of copper	0.5
Distilled water	100.0

This fluid has the advantage that preparations will harden in from eight to ten days; and if in the incubator, in from four to five days. Its disadvantages over Mueller's fluid are that it does not prevent shrinking as well and that there is frequently a precipitate in the tissues.

5. **Bichlorid of mercury** is of particular value in the fixation of cells and mitotic figures, but it has very little penetrating power. All the solutions that contain bichlorid have the drawback that there is a precipitation of mercury in the tissues that may be mistaken for pigment unless removed. These compounds may be dissolved by the addition of several drops of iodin to the 80 per cent. alcohol into which the specimens are put after having been washed. The iodin may be added to the alcohol in which the cut specimens are placed before being stained.

6. **Zenker's fluid.**

Bichlorid of mercury	5.0
Potassium bichromate	2.5
Sodium sulphate	1.0
Distilled water	100.0
Glacial acetic acid	5.0

The mercury and bichromate are dissolved in warm water and the sodium then added. It is best not to add the glacial acetic acid till the solution is ready to be used, as the acid rapidly evaporates.

After being in the fluid for twenty-four hours or less according to the size of the specimen, it is thoroughly washed in running water twelve to twenty-four hours and then hardened in alcohol. The tissue should be passed through 80 per cent. alcohol containing iodin so as to remove the precipitate of mercury that forms.

Tissues prepared in this way stain according to all methods. The chromatin figures are well preserved as well as the erythrocytes.

7. Osmic acid.—Its penetrating power is very slight, so very thin pieces of tissue, not more than 5 mm. in thickness, can be used.

A 1 per cent. watery solution is usually employed. It should be kept in the dark, and when the specimen is fixed, well washed. The paraffin method of imbedding should be employed, using chloroform or clove oil, as the celloidin will dissolve out the fat. In clearing do not use xylol, as it also dissolves fat.

8. Flemming's Solution.—

1 per cent. aqueous chromic acid solution..	15.0
2 per cent. aqueous osmic acid solution...	4.0
Glacial acetic acid......................	1.0

The small bits of tissue are left in the fluid one to three days, well washed for several hours, then hardened in increasing strengths of alcohol. Is used for karyokinetic figures and for fat. Stains best with watery safranin.

Hermann's fluid is a modification of the above. A 1 per cent. platinum chlorid solution is used instead of the chromic acid. The nuclear figures are especially well preserved. The method of employment is the same as with Flemming's.

DECALCIFICATION

General Rules.

The tissue must be well hardened before being put in the decalcifying fluid, otherwise it will be much altered. The formalin method is well adapted and small pieces should be used.

An excess of fluid should be used and it should be frequently changed. After complete decalcification the tissue should be carefully washed for two or more days. It must then be rehardened before it is ready to cut. The tissue is decalcified if it allows a needle to penetrate without meeting distinct resistance.

The following are the fluids commonly used:

1. Chromic acid and its salts. Mueller's fluid for small pieces of bones or embryonal bones. Is a very slow process. Can be hurried by placing in an incubator.

2. Saturated watery solution of picric acid. Requires about three weeks for embryonal bones. Larger and older pieces take several months. Can be hastened by adding 3 to 5 per cent. of nitric acid. To remove the picric acid, wash the tissue, then place in 95 per cent. alcohol to which several drops of a saturated watery solution of lithium carbonate have been added. The fluid becomes colored and more carbonate should be added till it remains completely clear.

3. Hydrochloric acid. When used in 1 to 10 per cent. solution it works quite rapidly, but injures the tissues. Is best used as:

Ebner's fluid:

Hydrochloric acid	2.5
Alcohol	500.0
Distilled water	100.0
Sodium chlorid	2.5

This method can be hastened by increasing both the hydrochloric acid and sodium chlorid to 5 per cent.

4. Nitric acid, in from 3 to 10 per cent. in water or formalin, is well adapted for bone tissue from adults. The alteration to the tissue is less than when corresponding solutions of hydrochloric acid are used.

Haug recommends the following on account of its more rapid and better action:

Nitric acid, c. p.	30.0 to 90.0
Absolute alcohol	700.0
Distilled water	300.0
Sodium chlorid	2.5

5. Phloroglucin. This protects the tissues from the action of the acid, so that very strong solutions may be used. It acts very rapidly; small pieces are decalcified in half an hour, larger ones in several hours.

A stock solution is made consisting of:

Nitric acid, c. p.	10.0 c. c.
Phloroglucin	1.0 gram.

This is carefully dissolved by warming; is best done under a hood. To this is added 100 c.c. of a 10 per cent. aqueous solution of nitric acid.

A more slowly working mixture is:

Phloroglucin	1.0
Nitric acid	5.0
Alcohol	70.0
Distilled water	30.0

Thoma's method is to:

1. Harden in Mueller's fluid or alcohol.
2. Decalcify in:

Alcohol	5.0
Nitric acid	1.0

   changing the solution very frequently.
3. Wash in alcohol.
4. Wash thoroughly in alcohol to which has been added an excess of calcium carbonate.

The decalcification requires from two to three weeks for large pieces. To remove the acid the tissue has to be in the carbonated alcohol from eight to fourteen days; should remain till there is no acid reaction with litmus paper.

6. Trichloracetic acid, used in 5 per cent aqueous solution and frequently changed, decalcifies in from five to seven days; generally with good results.

INJECTION

For the purpose of making them more easily studied the blood-vessels and other hollow structures may be filled with some injecting material that contains a stain. This procedure is not frequently used for pathologic purposes.

IMBEDDING METHODS

The purpose of imbedding is to give to a tissue a sufficient firmness to permit the cutting of thin sections. Two methods

are commonly employed, one with celloidin, the other with paraffin.

Celloidin has the advantage of not requiring heat, and can be used for larger pieces of tissue. On the evaporation of the alcohol and ether a comparatively solid mass remains.

Paraffin can be used for small pieces of tissues only. It also renders the specimen brittle so that it is frequently difficult to cut good sections. Although fluid when kept at the necessary heat, the paraffin becomes hard on cooling.

Celloidin Method.—In this process two solutions of celloidin of different thickness are employed—one of the consistency of syrup, the other of that of molasses. These solutions are made by adding to a mixture of equal parts of absolute alcohol and ether enough celloidin to give the desired consistency. The specimens must be thoroughly dehydrated in absolute alcohol and then placed in equal parts of absolute alcohol and ether for twenty-four to forty-eight hours. This latter step is not essential, but is advisable. From the alcohol the specimens are left in the thin celloidin at least twenty-four hours and in thick celloidin for a like period. If there is no hurry, the longer the time in each celloidin solution, the better will be the result. They are then placed on blocks, covered with thick celloidin, and allowed to harden. In the course of a few minutes, when the block can be turned upside down without the specimen sliding off, they should be placed in 80 per cent. alcohol. After remaining there for several hours they are ready to cut.

The blocks best adapted for use are those made out of vulcanite or hard paraffin. The latter are particularly convenient. A square of hard paraffin is cut up into blocks of various sizes and the tops roughened with a knife so as to give a better surface for the celloidin to ahdere to. Cork and wood are not well adapted, as after being in the alcohol for any length of time the tannic acid is extracted; it penetrates the specimen and interferes with its staining properties.

In cutting celloidin sections the knife is clamped at a very marked slant, so that as much of it as is possible will be used.

The blade and the specimen should be kept constantly wet with 80 per cent. alcohol. As the sections are cut they are lifted off the knife with a camel's-hair brush and placed in a dish containing water. This causes them to flatten out.

After the staining has been completed the sections are passed through graded alcohols to remove the water and are then placed in some fluid that will clear them. Clove oil should not be used, as it dissolves the celloidin. Bergamot, cedar oil, creosote, and xylol, alone or in combination with one part of carbolic to three parts of xylol, do not affect the celloidin.

Summary:

1. Dehydration in absolute alcohol.
2. Absolute alcohol and ether, āā . 1 to 3 days.
3. Thin celloidin .... 1 to 5 days.
4. Thick celloidin................. 1 to 5 days.
5. Mount on block.
6. 80 per cent. alcohol............ 12 to 24 hours.
7. Cut on microtome.
8. Stain, dehydrate, and clear.
9. Mount in balsam.

Paraffin Method.—The preparation must be thoroughly dehydrated in absolute alcohol or anilin oil. It is then placed in some fluid that is a solvent of paraffin—xylol or chloroform are commonly used—for four to five hours. The fluid should be changed several times. Then it is put in a mixture of chloroform or xylol and paraffin for two to three hours. The infiltration is hastened by heating the mixture at about 50° C. It is then placed in paraffin that melts at about 50° C. for three to five hours, the paraffin having been changed once or twice. The melting-point can be varied by making combinations of paraffin that melt at different degrees. The two generally used are one of 56° C. and another of 45° C. In warmer weather a paraffin with a higher melting-point is used.

The specimen is taken and placed in a little paper box in which a small amount of paraffin has been poured. When the tissue has been properly arranged more paraffin is added.

The box is then placed in a dish of cold water so that it will be rapidly cooled. This prevents crystallization and brittleness. Instead of using the paper boxes two right angles of metal are put on a glass plate so as to form an enclosure. Paraffin is poured in to form a thin film, then the tissue, and finally more paraffin.

After cooling, the specimen is fastened on a block of vulcanite or hard paraffin by heating its surface, and is then cut on the microtome. The blade is held at a right angle if the specimen is small, on a slant if large, and the cutting is done dry, no alcohol being used.

Summary of the paraffin imbedding:

1. Dehydration in absolute alcohol.
2. Xylol or chloroform four to five hours, changing the fluid a couple of times.
3. Xylol or chloroform and paraffin, two to three hours.
4. Melted paraffin in hot chamber at 50° C. for three to five hours. Change once.
5. Block and quickly cool.
6. Cut.

The paraffin sections are so brittle that they cannot be treated in the same way as the celloidin ones. The best method is to take the section and place it in a dish containing water at about 45° C. This causes the specimen to flatten. A perfectly clean slide is then smeared with a very fine film of glycerin-albumin and is slipped under the floating section. The excess of water is drained off or carefully touched with blotting-paper and the slide is then placed in the incubator at 37° C. for three to five hours.

The paraffin should be removed before staining the section. This is hastened by holding the slide over a small flame till the paraffin becomes transparent, when it is placed in xylol or turpentine for about two minutes. From there into absolute alcohol for about five minutes. It is advisable but not necessary to put the slides into weaker alcohol before beginning the stain. When the above steps have been gone through the tissues may be stained any way that is desired.

Glycerin-albumin solution for fastening paraffin sections to the slide is made as follows: The white of an egg is well beaten and to it is added an equal volume of glycerin. These are thoroughly mixed and filtered. It is used by smearing a very thin layer on the slide, the paraffin section is placed on it and then heated up to a temperature of about 60° C. till the albumin coagulates. If the sections have been taken from water it must be allowed to evaporate before the coagulating is done. The evaporation will be hastened by placing the slides in the incubator.

CUTTING SECTIONS

Freezing Microtome.—This method is valuable for rapid diagnostic work, but sections cannot often be cut sufficiently thin to allow a careful examination of the details.

The piece of tissue used should not be more than 4 mm. high and it must be free from all traces of alcohol. The alcohol is removed by placing the specimen in a large amount of water that is of a temperature of about 30° C.

The specimen is placed on the metal stand and a spray of ether or of carbonic acid gas is directed against the under side. The tissue is held in place by lightly pressing upon it with some flat piece of wood, as the handle of a small scalpel. Care must be taken not to freeze the tissue too hard or it will be so brittle as to break or show irregular streaks. The cut sections should be placed in 80 per cent. alcohol, as they will unroll better than if put directly into water.

The freezing method is particularly well adapted for tissues that have been hardened in Mueller's fluid, as there is no change in the finer characteristics. Formalin is very useful, as it permits very good sections to be made and is employed especially in the rapid diagnosis of tumors.

A rapid method is as follows:

1. Take a small portion of the tissue that has been removed at the operation and place immediately in a 10 per cent. solution of formalin for about two minutes.
2. Freeze, put the sections into water to flatten.
3. Stain in lithium carmin two to three minutes.

4. Blot stain and mount in glycerin.

Serial Sections.—*Paraffin.*—The block containing the specimen is turned till the anterior and posterior edges are parallel; as much of the paraffin being removed as is possible. The knife is placed at right angles and with rapid strokes of the knife the sections are cut. The edges of the sections cling to each other and long ribbons may be cut. These ribbons should be carefully placed on sheets of toilet paper, carefully numbered and marked, so that the beginning of each series can be determined. The ribbons are divided into lengths convenient for placing on the slide. They are then floated on water and picked up on the slide covered with the glycerin-albumin.

STAINING

The principle of staining depends upon the different affinity of certain portions of the tissue for special dyes, so that they become more evident for purposes of study. There are certain stains which show a distinct affinity for the nuclei, while others select the cell protoplasm and the intercellular substance. By employing two stains a double coloring is obtained. In some conditions a single color may affect different portions of the tissue differently.

According to their reaction, stains are divided into the basic, which are commonly nuclear or chromatin stains, and the acid, those that affect the cell protoplasm or the intercellular tissue. Neutral stains are generally artificial combinations of some of the above two.

After being stained it is generally well to differentiate. Although a stain may be a nuclear one, yet there is usually some effect upon the other substances, the same holding true in regard to the acid stains. To remove this color, certain fluids are used, as water, weak solutions of acid in water or alcohol, alcohol, anilin oil, and tannic acid.

It is also necessary that the sections shall be rendered transparent, and this is brought about by placing them in xylol, carbol-xylol, oil of clove, creosote, or bergamot.

Certain general rules should be observed:

1. All staining fluids should be filtered before use to avoid precipitates in the tissue. Good stains should be used, the best being those of Dr. Grübler, of Leipzig.

2. The sections should be spread out in the stain and should not lie upon each other, as the fluid is then likely to stain unevenly. Large amounts of stain in large dishes should be employed. Is is also an advantage to carefully move the sections to and fro.

3. The time required for staining varies, as a rule being less in old, well-ripened stains than in others freshly prepared. This depends also upon the proper hardening and fixation of the tissue, and also upon its age. Fresh tissues will stain more deeply and more quickly than old ones.

4. The staining of refractory tissues may be assisted by:
   (*a*) Concentration of the stain.
   (*b*) Staining for a longer time, up to twenty-four hours.
   (*c*) Heating up to 37° C.
   (*d*) Adding mordants, as acids and alkalies, anilin oil, etc.

5. The sections should be carefully washed in water to remove all traces of the decolorizing agents used.

6. Sections should be thoroughly dehydrated before being mounted, otherwise those areas containing water will not be transparent and will contain what appear to be oval pigment particles.

Method of staining and mounting sections:

1. Stain.
2. Wash, usually in distilled water.
3. 80 per cent. alcohol two to three minutes.
4. 95 per cent. alcohol three to five minutes.
5. Absolute alcohol two to three minutes.
6. Clearing fluid till the specimen sinks below the surface, two to three minutes.
7. Place section on slide, blot off the excess of clearing fluid, and mount in balsam, using a cover-glass.

NUCLEAR STAINS

Aqueous alum hematoxylin solution.

Hematoxylin crystals	1 gm.
Sat. aq. sol. ammonia alum	100 c.c.
Water	300 c.c.
Thymol	a crystal.

Dissolve the hematoxylin in a little water by the aid of heat. After the solutions have been mixed expose to the light and air in an unstoppered bottle for about ten days. Then tightly cork.

Delafield's hematoxylin.

Hematoxylin crystals	4 gm.
Alcohol (95 per cent.)	25 c.c.
Sat. aq. sol. ammonia alum	400 c.c.

Dissolve the hematoxylin in the alcohol, then add the alum solution. Expose the mixture to the air and light four to five days. Then filter and add:

Glycerin	100 c.c.
Alcohol (95 per cent.)	100 c.c.

Expose to light and air for a couple of weeks, then filter and keep tightly corked. The solution lasts well and stains the more rapidly the older it gets.

Ehrlich's acid hematoxylin.

Hematoxylin crystals	2 gm.	
Absolute alcohol	60 c.c.	
Glycerin	60 c.c.	saturated with ammonia alum.
Water	60 c.c.	
Glacial acetic acid	3 c.c.	

The solution is ripened in an uncorked bottle till it becomes deep red in color; requires a couple of weeks. If kept in well-stoppered bottle precipitates do not form and the solution retains its staining powers for years. Also does not overstain.

Mayer's hematein. When hematein is used, ripening is unnecessary, but the results from such stains are not as satisfactory as when hematoxylin is used:

Hematein	0.4 gm.
(Dissolve in a few drops of glycerin)	
Alum	5.0 gm.
Glycerin	30.0 c.c.
Water	70.0 c.c.

Hematoxylin Staining.—The nuclei are stained blue. The older the solutions, the quicker they act and the deeper they stain. If the sections are overstained, the excess of color can be removed by placing them in hydrochloric acid alcohol till the proper color is obtained. The acid causes the blue to change to a brown, but the color is regained when the sections are placed in water. The acid should be thoroughly washed out; this can be hastened by using water to which an equal amount of a saturated watery solution of lithium carbonate has been added.

1. Stain three to ten minutes according to age of stain.
2. Wash thoroughly.
3. Differentiate with acid alcohol, about thirty seconds if sections are overstained.
4. Wash thoroughly.
5. A counter-stain, eosin, is usually employed.
6. Dehydrate, clear, and mount in balsam.

Alum carmin.

Carmin	1 gm.
5 per cent. alum solution	100 c.c.

Boil for one-half to one hour and when cool filter. It stains the nuclei a violet red. There is no danger of overstaining and the color is not very easily removed in water or weak acid solutions. This preparation does not work well with objects that are difficult to stain.

The sections are placed:

1. In the stain for ten minutes to two hours.
2. Then washed thoroughly in distilled water.

3. Dehydrated in alcohol, cleared and mounted.

Lithium carmin.

Carmin	2.5 to 5.0 gm.
Sat. sol. lithium carbonate	100.0 c.c.

Heat and filter. The nuclei are stained an intense red. Is well adapted for tissues that stain with difficulty. Any excess of color can be removed in acid alcohol. Is a good counter-stain for tissues that have been injected with blue substances.

Sections are placed:

1. In the stain for two to three minutes.
2. Washed in water.
3. Differentiated for one-half to one minute in acid alcohol; hydrochloric acid 1, 70 per cent. alcohol 100.
4. Washed thoroughly so as to remove the acid.
5. Dehydrated in alcohol, cleared, and mounted in balsam.

Picro-lithium carmin.

Lithium carmin solution	1 part
Sat. watery sol. picric acid	2 parts

Sections are

1. Stained three to five minutes.
2. Washed.
3. Differentiated two to three minutes acid alcohol.
4. Washed thoroughly.
5. Dehydrated in alcohol that has had a little picric acid added to it.
7. Cleared and mounted.

Nuclei are stained brownish-red, and the protoplasm yellow.

Borax carmin.

Carmin	0.5 gm.
Borax	2.0 gm.
Distilled water	100.0 c.c.

Mix and heat till boiling begins; should be stirred constantly; then add 4.5 parts of dilute acetic acid (0.5 per cent.) and let stand twenty-four hours; then filter.

This gives the same results as the lithium carmin except that the color is not so intense.

Sections placed:

1. In stain for five to fifteen minutes.
2. Washed in water.
3. Differentiated one-half to one minute in acid alcohol solution.
4. Washed in water thoroughly to remove acid.
5. Dehydrated, cleared, and mounted.

Bismarck brown.

Either a 3 to 4 per cent. watery solution obtained by boiling and filtering.

Or a concentrated alcoholic solution made in 40 per cent. alcohol, equal to 1½ to 2 per cent.

Sections are:

1. Stained five minutes.
2. Washed in alcohol or 1 per cent. hydrochloric acid alcohol.
3. Dehydrated, cleared, and mounted.

The nuclei are stained a deep brown, the protoplasm a lighter color. Bacteria are an intense brown. Cannot overstain. This method is especially adapted for micro-photographic work.

Gentian-violet. Either a 1 per cent. watery or a 2 per cent. alcoholic solution may be used. Are likely to overstain.

Sections are:

1. Stained three to five minutes.
2. Washed in alcohol till they become a pale blue.
3. Then in absolute alcohol.
4. Cleared and mounted.

The nuclear staining is clearer if the sections are put for fifteen to thirty seconds in a ½ per cent. solution of acetic acid and then into the alcohol.

Safranin.—Is usually employed after fixing in Flemming's solution to bring out karyokinetic figures.

Sections:

1. Stained one-half to twenty-four hours in a 1 per cent. watery solution of safranin.
2. Quickly washed in water.
3. Washed in absolute alcohol to which 5 to 10 drops of 1 per cent. hydrochloric acid alcohol have been added.
4. Washed in pure absolute alcohol till the section is a clear brown.
5. Cleared and mounted in alcohol.

The resting nuclei are pink, those undergoing mitotic changes are deep red.

Another method is:

Anilin oil	2.0 c.c.
Water	100.0 c.c.
Safranin in excess.	

Heat to 60° C. and filter. The solution will last about two months. This form stains almost immediately. The after-steps are as above.

DIFFUSE AND DOUBLE STAINING

Double staining is employed for the purpose of obtaining a contrast between the nuclei and the plasms and interstitial substance. The nuclear stain is employed first, as the contrast stain is weaker and colors the tissues more diffusely.

Neutral Carmin.

Carmin powder	5.0 gm.
Aq. ammon. fort	1.0 c.c.

These rubbed together then add:

Distilled water	200.0 c.c.

Boil till the ammonia is driven off. Allow the solution to stand uncorked for about a week, then filter. The solution works better as it becomes older.

To prepare the stain for immediate use add just enough ammonia to the carmin to make a paste. This should be thinly spread on the sides of the mortar and allowed to dry. Pulverize again, let it remain exposed to the air for twenty-four hours, then dissolve in cold water; it is then ready for use.

To stain sections: Add the stock solution to distilled water until a clear pale red color results. The sections remain in this until they become plainly red, up to twelve hours. The best results are obtained by staining for a long time in a weak solution. Strong solutions stain more rapidly. Wash thoroughly in water, dehydrate, clear and mount.

The counter-stain best used is hematoxylin, and it should be employed first.

Eosin.—Either the form soluble in water, which is the better, or that in alcohol may be used. A few drops of a concentrated solution of either variety is added to a small dish of water and the sections stained till they are of a reddish color—one to three minutes.

Then washed in water.

Dehydrated in alcohol. Should be careful not to leave in the alcohol too long, as it gradually dissolves out the stain.

Cleared and mounted.

This method is preceded by staining in hematoxylin. In such cases the nuclei are blue. In specimens fixed in formalin or sublimate solutions the red blood-cells stain a bright red or copper color and the blood-vessels are prominent. Eosinophile cells show up plainly. The other tissues show a diffuse reddish tinge.

Picric acid is generally used in combination with some other stain, as in Van Gieson's method. As the picric acid decolorizes the sections, they should be overstained in the hematoxylin. If iron hematoxylin is used instead of Delafield's, the decolorization does not occur to the same extent.

Van Gieson's method for nervous tissue:

1 per cent. aqueous sol. acid fuchsin	15 c.c.
Sat. aq. sol. picric acid	50 c.c.
Water	50 c.c.

For connective tissue:

1 per cent. aq. sol. acid fuchsin...........	5 c.c.
Sat. aq. sol. picric acid..................	100 c.c.

Sections are:

1. Overstained in Delafield's hematoxylin.
2. Washed thoroughly in water.
3. Stained in Van Gieson solution three to five minutes.
4. Washed in water one-half minute.
5. Dehydrated, cleared, and mounted.

Nuclei are stained brownish-red; connective tissue, varying shades of light red; axis-cylinders, brownish-red; myelin sheaths, yellow; neuroglia and sclerosed fibers, red; amyloid, rose or reddish-brown; hyaline, red; colloid, orange or red.

CONNECTIVE TISSUE STAINS

Van Gieson's stain, as already given, may be used. The best results are obtained after fixation in chrome salts or sublimate solutions; are not so good after alcohol.

Mallory's anilin blue stain gives good results after fixation in Zenker's fluid or sublimate solutions. The fibrillæ and reticulum of connective tissue, amyloid, mucous, and other hyaline substances stain blue; the connective tissue can be differentiated from the other substances by their form. Nuclei, protoplasm, fibroglia fibrils, axis-cylinders, neuroglia fibers, and fibrin stain red; erythrocytes and myelin sheaths yellow; elastic fibers pale pink or yellow.

Sections are:

1. Stained in a $\frac{1}{10}$ per cent. aqueous solution of acid fuchsin five or more minutes.
2. Transfer to the following solution and stain twenty minutes or more:

Anilin blue soluble in water (Grübler)....	0.5 gm.
Orange G. (Grübler)....................	2.0 gm.
1 per cent. aqueous solution of phosphomolybdic acid..........................	100.0 c.c.

3. Wash and dehydrate in several changes of 95 per cent. alcohol.
4. Clear in xylol or in oil of origanun (Cretici).
5. Balsam.

ELASTIC FIBER STAIN

Weigert's stain for elastic fibers. It is best to buy the stain already made up, as its preparation is rather difficult.

The sections are:

1. Stained in the above solution for twenty minutes to an hour.
2. Washed off in alcohol.
3. Blotted with filter-paper, xylol added, and blotted two or three times till the section is clear.
4. Mounted in balsam.

The elastic fibers are dark blue, almost black.

Unna's orcein stain.

Orcein	1 gm.
Hydrochloric acid	1 c.c.
Absolute alcohol	100 c.c.

Sections are:

1. Stained six to twenty-four hours.
2. Washed thoroughly in 70 per cent. alcohol.
3. Washed in water to get rid of the acid.
4. Dehydrated, cleared, and mounted.

The elastic fibers are a deep silky brown color, connective tissue a pale brown. This method has the advantage that elastic fibers that have degenerated into elacin take the basic blue stain.

BLOOD STAINING

Before being stained the blood must be fixed to the slide either by heat or by some chemical.

Heat may be used in all cases except when Wright's stain is employed; it must be used with Ehrlich's triple stain to get good results. The films should be exposed to a dry heat of from 100° C. to 110° C. for ten to fifteen minutes.

Chemicals.—The smears are fixed in absolute alcohol or ether or a mixture of equal parts of the two for five to ten minutes. Then dried and stained.

Stains.—*Wright's.*—Is best to procure this stain ready-made. It is employed as follows, as no previous fixing is necessary:

The unfixed film is covered with the solution and stained for a minute. Distilled water is added drop by drop till a metallic scum appears on the surface of the fluid and is allowed to remain two to three minutes. Then wash the film, which is deep blue or purplish color, till it becomes yellowish or pink. Dry between blotting-paper and mount in balsam.

The erythrocytes will be stained orange or pink; the nuclei of the leukocytes, blue; neutrophile granules, lilac; eosinophile granules, pink; fine basophile granules, deep blue; coarse mast cell granules, deep purple. The malarial organism stains blue.

Ehrlich's Triacid.—Best bought ready-made.

After fixing with heat, stain five to eight minutes, wash in running water, dry and mount.

Erythrocytes stain orange; nuclei of the leukocytes, greenish-blue; neutrophile granules, violet or lavender; eosinophile granules, copper red; basophile granules are unstained.

Polychrome Methylene-blue (Goldhorn's).—Is bought ready-made.

After fixation for fifteen to twenty seconds in methyl-alcohol, wash in water and, without drying, stain for one to two minutes. Wash thoroughly in running water, dry with blotting-paper, and mount.

This method shows very well granular degenerations of the erythrocytes, the nuclei of erythroblasts and leukocytes, basophilic granules, and most bacteria. It is a very good stain for the malarial organism. If the film is first stained for ten to fifteen seconds in a 0.1 per cent. aqueous solution of eosin, washed, and then the methylene-blue used, a very good picture of the acid coloring elements is given.

Eosin and Methylene-blue.—Fix the smear in absolute

alcohol alone or mixed with an equal quantity of ether. Stain in a 0.5 per cent. solution of eosin in absolute alcohol, to which an equal quantity of water is added, for about five minutes without heating. Wash and dry, then counterstain in a saturated aqueous solution of methylene-blue for about one minute. Wash again, dry and mount.

Gives a good picture of the nuclei of the basophilic granules and of the malarial organism; eosinophile granules stain red; the protoplasm of the polymorphonuclear leukocytes colors a slight pink, the granules remaining unstained.

CHAPTER XVII

BACTERIOLOGICAL METHODS

CULTURE MEDIA

These consist of various nutritive substances employed for the cultivation of bacteria. They may be liquid or solid.

Bouillon.—This medium is used by itself and also as the nutritive basis of certain solid media. It may be made up with lean beef or with 3 grm. of beef extract. If the former is used is must be freed from fat and gristle and finely minced. Five hundred grams of it are mixed with 1000 c.c. of water and boiled for about half an hour. It is then filtered and to the clear filtrate is added 10 grm. of Witte's pepton, 5 grm. of sodium chlorid, and enough water to bring the quantity up to 1000 c.c. This mixture is boiled till everything is dissolved, and it is then neutralized, as its reaction is very acid.

The neutralization should be very carefully carried out so that the final reaction is slightly alkaline. This is done by carefully adding a 10 per cent. solution of caustic soda and testing with litmus paper. During this process the solution is kept boiling. When the reaction has been obtained filter and add enough water to bring the volume up to 1000 c.c. The bouillon frequently becomes cloudy on account of a precipitate of phosphates. If this occurs, a permanently clear fluid may be had by refiltering.

Glucose bouillon is similar to the above except that it contains 1 per cent. glucose in addition.

Agar-agar.—To 1000 c.c. of beef bouillon 15 grm. of agar-agar are added and boiled for an hour, constantly stirring. Water is added at various intervals to keep up the required volume. After the boiling is done the contents are

allowed to cool to 60° C., at which point an egg is beaten into the fluid, which is again boiled for about ten minutes. Then filter while hot through wet filter-paper. A jacketed filter kept warm by a gas flame facilitates the process. As the fluid cools while filtering it has to be again heated till all passes through.

The purpose of the agar-agar is to give a medium that will remain solid at a temperature equal to that of the body, which is the best for many bacteria. The agar will melt at about 42° C.

Gelatin.—To 1000 c.c. of boiling beef bouillon add 100 grm. of golden seal French gelatin. When the gelatin is thoroughly dissolved boil for about five minutes and neutralize by the method described for bouillon. The mixture is cooled to 60° C., an egg beaten in, boiled about ten minutes, and filtered through wet filter-paper. Should add sufficient water to bring the quantity up to the original amount. It may have to be re-heated a couple of times before filtration is complete. Care must be taken not to bring the mixture to the boiling temperature more frequently than is necessary, as the power of coagulation may be destroyed.

This medium melts at temperatures above 22° C.

Glucose gelatin is gelatin that has been dissolved in glucose bouillon.

Blood-serum (*Loeffler's Mixture*).—The blood-serum is obtained by collecting it at a slaughter-house. Jars holding about a gallon should be used. These should be clean but not necessarily sterilized. The collected blood is put aside in a cool place for twenty-four to forty-eight hours till the blood is completely clotted. If the clot adheres to the side of the jar, loosen it with a glass rod. The clear serum is removed with a pipette. This is then mixed with glucose bouillon.

Glucose bouillon (1 per cent.)............	1 part
Beef blood-serum......................	3 parts

The above is then run into test-tubes to a depth of about 4 cm. These are placed on an incline so that they will be on a slant when coagulated. In this position they are placed

in a hot-air sterilizer and kept at a temperature between 85° and 90° C. for an hour. The thermostat should be carefully watched so as to not have the heat vary from the above figures. After the medium has become thoroughly coagulated the tubes are sterilized in steam for half an hour on three successive days.

Litmus Milk.—To milk that has been freed from cream enough of a freshly prepared aqueous solution of litmus is added to give it a blue color. This is run into test-tubes which are treated by intermittent steam sterilization. Fresh milk should be used and the process quickly carried out to prevent as much as possible the growth of bacteria.

Potato Cultures.—The potatoes should be thoroughly scrubbed with brush and water. Solid cylinders of a size to fit the test-tubes are cut with a cork borer. They are then split obliquely and the pieces placed in running water for some twelve hours. The oblique pieces are then placed in test-tubes with the larger end downward. A few drops of water should be added to prevent drying. The tubes are then put through the fractional steam sterilization.

Dunham's Pepton Solution.—

Pepton	10 grm.
Sodium chlorid	5 grm.
Distilled water	1000 c.c.

The pepton and sodium chlorid are dissolved by boiling and the mixture filtered. Test-tubes are filled and sterilized.

Filling of Test-Tubes.—New test-tubes are best cleaned by washing in a very weak solution of nitric acid, then rinsing in water and allowing to become dry or nearly so. Old tubes that have contained cultures are boiled for nearly an hour in a 6 per cent. solution of common soda.

The cleaned tubes are plugged with *raw* cotton, placed in the hot-air sterilizer at 150° C. till the cotton has turned brownish. This is to mold the stopper to the shape of the tube.

To fill the tubes it is best to take a large funnel and by means of a short piece of rubber connect it to a piece of glass tubing a couple of inches in length. The supply of the me-

dium is controlled by a pinch-cock on the rubber. The glass tube is inserted into the test-tube, the required amount of medium run in, and the cotton plug put back. Care should be taken not to get any of the culture medium on the neck of the tube, as the cotton would stick to it. If "slant" cultures are to be made, run in about 5 c.c. of fluid; if "stab" cultures, about 8 to 10 c.c. should be used. The filled tubes are then sterilized.

Instead of test-tubes, flasks of varying sizes may be used to contain the medium.

Sterilization of Culture Media.—This may be done by the intermittent method. In this the media are exposed to steam on three successive days for a period of thirty to forty-five minutes. A single sterilization will kill all bacteria except those that are in the spore stage. These bodies will, however, develop within the twenty-four hours into the adult form, and are then killed by the subsequent sterilization.

Instead of the above the autoclave may be used. It is a metal chamber so arranged as to allow sterilization under pressure. A temperature of 110° C. is obtained, and in it all bacteria and spores are destroyed in twenty to thirty minutes.

After the final sterilization if "slant" cultures are to be made the test-tubes are so placed that the medium will come about half-way up the side of the tube.

When the media have solidified the tubes can be kept a longer time if the cotton is trimmed off and rubber caps put on.

Sterilization of Apparatus.—Metal bodies that will not be injured, platinum wires, forceps, etc., may be placed directly in the flame of a Bunsen burner. Glassware is sterilized by hot air, by steam, or by boiling. Chemical sterilization is not often employed.

Forms of Cultures.—

1. Slant.
2. Stab.
3. Petri dish.
4. Esmarch tube.
5. Hanging drop.
6. Anaërobic.

1. Slant cultures: A platinum wire is taken and heated in the flame. When cool it is inserted into the material to be examined. Then without touching anything, not even the sides of the tube, the point of the wire is carefully drawn over the surface of the medium and the wire again sterilized. When the cotton plug is removed, the end of the tube should be passed through the flame. Care should be taken at all times that the platinum wire is carefully sterilized before being laid anywhere.

2. Stab cultures are made by carefully inserting the platinum wire, which should be straight, into the center of the culture media. The same precautions as mentioned above should be observed.

3. The Petri dish consists of a shallow glass dish with a cover. It is used to a large extent for the purpose of isolating colonies and obtaining pure growths. The tubes inoculated directly from the material examined usually contain several varieties of organisms. The method of isolating is as follows: Three tubes of agar-agar or gelatin are melted and then placed in a water-bath at a temperature between 40° and 42° C. A platinum wire with a small loop at the end is inserted into the infected substance and then a tube is inoculated. From this tube a loopful is carried over to tube No. 2, and a third tube is inoculated from the second, the platinum wire being sterilized each time. Three sterile Petri dishes are taken and a tube is inserted under the cover of one and its contents poured out. This is done with all three, care being taken to have the medium evenly distributed over the bottom of the dish. They are then grown twenty-four hours.

The first tube will contain so many organisms that Petri dish No. 1 will be covered with colonies. The second tube, being diluted, will give fewer colonies on dish No. 2, while dish No. 3, obtained by pouring out tube No. 3, will have only a few scattered colonies. From this last dish the individual growths may be removed with a sterilized platinum-needle and inoculated into a fresh tube, a pure culture thus being obtained.

4. The Esmarch tube is made by taking an inoculated tube

of melted agar or gelatin, laying it on a block of ice, and rotating till the medium is distributed in a thin coat on the inside. Care must be taken that the contents do not come in contact with the cotton plug. This method has been practically supplanted by the Petri dishes.

5. Hanging drop cultures are obtained by taking a slide in which there is a depression and a ring of vaselin is made around it. A sterilized cover-glass is taken, a drop of bouillon placed on it, and this is inoculated with the usual precautions. The cover-glass is inverted over the depression in the slide and pressed down upon the vaselin. This is put in the incubator for twelve to twenty-four hours and then examined.

6. Anaërobic cultures may be made in various ways. A test-tube half full of solid medium is inoculated while still fluid or by a deep stab inoculation when cold. The bacteria in the deeper portions will be without air. Melted paraffin or oil may be poured in the tube to keep out air. Pyrogallic acid in combination with strong sodium hydrate is also used. The oxygen within the tube may be replaced by an atmosphere of hydrogen and the tube then sealed.

STAINING BACTERIA

Staining Cover-glass Preparations.—A well-cleaned cover-glass has a small portion of the material for examination spread out on it in a very thin layer by means of a sterilized platinum wire. The preparation is allowed to dry; is best not to do it over a flame. When dry the cover-glass is passed rather slowly three times through the flame of a Bunsen burner. This coagulates the albumin and prevents the material being washed off during the process of staining. The cover-glass is covered with the stain and gently warmed for fifteen to twenty seconds over a small flame. The specimen is then washed in water, dried by blotting and by gently warming, and mounted in balsam.

Various of the anilin colors are the ones chiefly used in bacterial staining. They may be used alone or in combination with certain reagents employed to increase the staining power.

Saturated alcoholic solutions of the stains should be kept in stock and from them the dilute aqueous solutions can be prepared. These latter, however, do not keep well, so various standard preparations are usually kept on hand.

Loeffler's Methylene-blue.—

Sat. alc. sol. methylene-blue.............. 30 c.c.
Caustic potash in water, 1:10,000........100 c.c.

This keeps a long time and stains rapidly.

Gabbet's Methylene-blue.—

Methylene-blue.......................... 2 gm.
Sulphuric acid..........................25 c.c.
Water...................................75 c.c.

This is employed as a contrast stain and a decolorizer for tubercle bacilli.

Carbol-fuchsin.—

Sat. alc. sol. fuchsin.....................10 c.c.
5 per cent. watery sol. carbolic acid.......90 c.c.

This stain is very permanent and is useful for many purposes. Is employed in the differential diagnosis of tubercle bacilli. In this method (Ziehl-Nielson) the cover-glass or slide is covered with the above stain and heated, till steam rises, for about three minutes. Care must be taken not to boil the stain, and to replace the solution as it evaporates. Wash thoroughly in water and then decolorize with about a 10 or 15 per cent. watery solution of nitric or sulphuric acid. Wash again in water and counter-stain for a minute in Loeffler's methylene-blue. The tubercle bacilli will appear as minute red rods; all other organisms will be blue.

Anilin Gentian-violet.—

Sat. alc. sol. gentian-violet...............16 c.c.
Anilin water...............................84 c.c.

Anilin water is made by taking:

Anilin oil............................... 5 c.c.
Distilled water..........................95 c.c.

Shake thoroughly till a milky fluid is obtained; then filter.

This stain should be freshly prepared when needed, as it does not last more than ten days.

Gram's Method.—After the cover-glass has been smeared and fixed it is stained in:

1. Anilin gentian-violet thirty seconds.
2. Washed in water two or three seconds.
3. Put in Gram's solution, as follows, for thirty seconds.

Iodin	1 gm.
Potassium iodid	2 c.c.
Water	300 c.c.

4. Washed in 95 per cent. alcohol till the color ceases to come out of the preparation.
5. Dry by blotting and in air and mount in balsam.

The value of this method lies in the fact that certain bacteria will retain the stain while others give it up. The bacteria stain dark blue or black while the nuclei are only faintly colored. Nuclei that are undergoing division may stain rather deeply.

An organism is said to stain by Gram's method when it is not decolorized. This power is made use of to differentiate certain organisms that may resemble each other in size and shape.

The more important pathogenic bacteria are divided as follows, according to their reaction to Gram's:

Stained by Gram's Method.	Decolorized by Gram's Method.
Staphylococcus pyogenes.	Gonococcus.
Streptococcus pyogenes.	Bacillus typhosus.
Streptococcus capsulatus.	B. coli communis.
Actinomycosis.	B. malignant œdema.
Bacillus anthracis.	Spirillum of Asiatic cholera.
Pneumococcus.	Diplococcus intracellularis meningitidis.
B. diphtheriæ.	B. pyocyaneus.
B. lepræ.	B. of influenza.
B. tuberculosis.	B. of dysentery.
B. tetanus.	B. of bubonic plague.
B. aërogenes capsulatus.	B. of glanders.
	Spirochæta of relapsing fever.

METHODS FOR STAINING SPORES

Spores are the resting forms of various organisms and are stained with difficulty, but when once stained are hard to decolorize.

Abbott's Method.—

1. Stain the cover-glass deeply with methylene-blue, heating till the solution boils.
2. Wash in water.
3. Wash in 95 per cent. alcohol, containing 0.2 to 0.3 per cent. HCl.
4. Wash in water.
5. Stain for eight to ten seconds in anilin-fuchsin solution.
6. Wash in water, dry and mount.

The spores are stained blue, the bodies of the bacteria red.

Moeller's Method.—

1. Wash the cover-glass for two minutes in chloroform.
2. Wash in water.
3. Place in a 5 per cent. watery solution of chromic acid for one-half to two minutes.
4. Wash in water.
5. Stain with carbol-fuchsin for one minute, heating the solution slowly till it boils.
6. Thoroughly decolorize in a 5 per cent. solution of sulphuric acid.
7. Wash in water.
8. Stain in aqueous methylene-blue (1 gram to 100 c.c.) for thirty seconds.
9. Wash in water, dry and mount.

The spores will be red and the bacteria blue.

STAINING OF FLAGELLA

Loeffler's Method.—

1. Flood the cover-glass with the following solution, which should be filtered before using:

20 per cent. aqueous solution of tannic acid	10 c.c.
Cold saturated solution of ferrous sulphate	5 c.c.
Saturated aqueous or alcoholic solution of gentian-violet or fuchsin.............	1 c.c.

This is very gently heated, not boiled, for about one minute.

2. Wash in water.
3. Stain in anilin gentian-violet or anilin-fuchsin with gentle heating thirty to sixty seconds.
4. Wash, dry, and mount.

Bowhill's Method. — Stain the cover-glass in the following solution, heating gently for ten to fifteen minutes:

Saturated alcoholic solution of orcein......	15 c.c.
Aqueous solution of tannin (20 : 80)......	10 c.c.
Distilled water........................	30 c.c.

Filter the mixture before using. The orcein stain should be at least nearly two weeks old.

In staining sections for bacteria Gram's method or that used for the tubercle bacillus is generally employed. Better results are obtained with paraffin sections, but celloidin may be used.

Staining Capsules.—

1. Cover the preparation with glacial acetic acid for a few seconds.
2. Drain off (do not wash) and replace with anilin gentian-violet. Pour this off and add more stain till all of the acid has been removed.
3. Wash in a 2 per cent. solution of sodium chlorid and examine in the same.

PART II—SPECIAL PATHOLOGY

CHAPTER XVIII

THE BLOOD

Blood is composed of two parts, the *cellular* elements, and the fluid or *liquor sanguinis.* Is alkaline in reaction, its specific gravity is about 1.055, and it has a characteristic odor in different animals.

The *arterial* blood is freshly aërated and is bright red in color, *venous* blood is bluish and does not contain oxygen, while capillary blood is intermediate.

The gaseous constituents and their proportions are as follows:

	Arterial.	Venous.
Oxygen	21.6	6.8
Carbon dioxid	40.3	48.0
Nitrogen	1.8	1.8

Erythrocytes.—Are bi-concave discs of an average diameter of 7.2 to 7.8 μ and are non-nucleated in their normal condition. Are very elastic, and are short-lived. Their function is to carry oxygen from the lungs to the tissues. They may vary greatly in health in both size and shape. *Microcytes* when below 4 μ; *megalocytes* or *macrocytes* when above 10 μ; these latter are found in pernicious anemia. *Poikilocytes,* those cells whose shape is much changed, usually pear-formed or stellate. When many are found the condition is known as *poikilocytosis.* Occur in severe anemias. At times may be nucleated. *Normoblasts* are nucleated reds the size of the usual erythrocytes. Are supposed to be corpuscles

that have been sent out before they have become fully matured, indicate an attempt at rapid regeneration. *Megaloblasts* are those from 9 to 14 μ in diameter. Nuclei may be multiple, may show degenerative changes. *Microblasts* are those from 2 to 5 μ.

Variations in number of the red cells are not uncommon. Normally have in a cubic millimeter five million in the male and four and a half million in the female. The number is diminished in women during menstruation, child-birth, and lactation. There are also variations during different times of the day. May be relatively increased when the blood is concentrated, as in profuse diarrheas; is called *polycythemia*. When decreased, as after severe hemorrhages, is known as *oligocythemia*.

According to Cabot, it takes from fifteen to thirty days to regenerate a loss of 4 per cent. of the blood in the body.

Hemoglobin.—The amount of the coloring-matter may be much diminished by loss of erythrocytes or by each cell containing less than its normal amount. Cells that have lost all their coloring-matter are known as *shadow corpuscles*. Diminution in amount is known as *oligochromemia*. Sometimes the hemoglobin may be dissolved in the plasma, *hemoglobinemia*. Occurs in various forms of poisoning as a result of destruction of the erythrocytes.

The amount of hemoglobin may be estimated in various ways by special instruments devised for the purpose. Its presence is recognized by the spectroscope. For the latter a 1 per cent. solution is used. This also shows the form present. *Methemoglobin* gives a chocolate color to the blood; is seen in potassium chlorate poisoning. In carbon monoxid poisoning the blood is a cherry-red. Is dark in color in carbon dioxid poisoning.

Leukocytes.—Are nucleated blood-cells that do not contain hemoglobin and vary in size from 5 to 10 μ. Usually have about 8000 in a cubic millimeter.

They may be divided as follows according to the way in which they react to stains, especially Ehrlich's:

The *polymorphonuclear* or *neutrophile* leukocytes con-

stitute about 70 per cent. of the white cells. They are about 10 μ in diameter and have nuclei that appear lobulated.

The cytoplasm contains small granules that stain purple or violet. These cells possess the power of ameboid motion and are also phagocytic.

The *small lymphocyte* is about the size of a red cell and has a round nucleus that almost competely fills the cytoplasm. Forms about 20 per cent. of the leukocytes. Does not contain granules. Is not ameboid.

The *large mononuclear lymphocyte* closely resembles the small, but it is slightly larger and contains a nucleus that is more oval and which does not stain so deeply as in the small variety. This form constitutes from 2 to 4 per cent. of the leukocytes. It also contains more cytoplasm than dose the small.

The *transitional* cell resembles the large mononuclear except that the nucleus is indented. It apparently represents a transition stage between the large lymphocyte and the polymorphonuclear leukocyte. Constitutes from 2 to 4 per cent.

The *eosinophile* is a leukocyte that is characterized by the presence in the cytoplasm of large coarse granules that stain deeply with eosin. The nucleus is usually polymorphic. Are ameboid. Constitutes from 0.5 to 4 per cent.

The *basophiles* are very seldom found. Cytoplasm contains fine granules that stain with basic anilin dyes. May be mononuclear or polymorphonuclear. Are known as "mast" cells when large, coarse, basophilic granules are present.

The *myelocyte* is a bone-marrow cell that is never seen in the normal blood. It is usually somewhat larger than the leukocyte and contains a large round oroval nucleus that stains very faintly. In the cytoplasm are large numbers of neutrophilic granules, as a rule, although in some cases they may show a marked affinity for eosin.

There may be marked variations in the number of leukocytes. Increase of the polymorphonuclear is called *leukocytosis*. *Lymphocytosis*, an increase of lymphocytes; *eosinophilia*, of eosinophiles.

Leukocytosis is a temporary condition, seen normally in the new-born, in pregnancy, after cold baths, and about three hours after eating.

Pathologic leukocytosis is seen particularly as a result of infection by pyogenic bacteria. In croupous pneumonia may get as high as 100,000 per cubic millimeter. Occurs after hemorrhages, in malignant disease, and just before death.

Lymphocytosis occurs in marasmus, syphilis, phthisis, in anemia, scurvy, and leukemia.

Eosinophilia is found most marked in parastitic diseases, gonorrhea, sarcoma, gout, bronchial asthma, disturbances of the sympathetic system, and in some forms of leukemia.

Leukopenia indicates a diminution in the number of the leukocytes.

Blood plates or placques are small, oval or round, colorless and flat bodies, seldom more than 3 μ in diameter. They are very viscid, are of high specific gravity, and are thought to be important in the formation of fibrin. Estimated at from 1,500,000, to 5,000,000 per cubic millimeter. Stain readily with anilin dyes. May be formed from erythrocytes.

DISEASES OF THE BLOOD

Pernicious anemia is a condition in which the amount of hemoglobin is diminished as well as the number of red cells and there appear in the blood many malformed erythrocytes.

Frequently the cause is unknown, but in some cases it may result from the presence of intestinal parasites, as the dibothriocephalus latus or the uncinaria duodenalis. It may occur as a result of numerous hemorrhages, of gastric carcinoma, and of infectious diseases.

The blood shows a marked diminution of erythrocytes, often as low as 1,000,000 or even 143,000; the hemoglobin is considerably reduced, 30 to 35 per cent., but the relative amount in each cell is high.

There are marked changes in the size of the erythrocytes, megalocytes being very numerous, also in shape, poikilocytosis. Nucleated red cells occur in quite large numbers,

megaloblasts particularly, although in some cases normoblasts predominate. The nuclei are frequently degenerated and generally show polychromatophilia.

The leukocytes are little involved until toward the fatal termination, when there may be extreme leukocytosis.

FIG. 111.—PERNICIOUS ANEMIA (Cabot).
L, L, Lymphocytes; m, m, m, m, megaloblasts; cover-slips stained with Ehrlich's triacid, and drawn with camera lucida.

Coagulation is slight, specific gravity is low, 1.028, and there is little tendency to form rouleaux.

The chief lesion of the tissues is an extreme fatty degeneration. The bone-marrow is red, soft, and frequently shows areas of hemorrhage. Microscopically nucleated red cells are seen in great numbers.

In the spinal cord degeneration of the posterior columns has been recognized.

Chlorosis is a blood disease occurring mainly in girls at the age of adolescence. It is characterized by a great reduction in the amount of hemoglobin without a corresponding reduction in the number of erythrocytes.

The cause is unknown. In some cases hypoplasia of the arterial system and of the genitalia has been observed.

FIG. 112.—MYELOGENOUS LEUKEMIA (Cabot).

a, Eosinophilic myelocytes; *b*, "mast-cell"; *e*, *e*, *e*, ordinary eosinophile; *m*, *m*, myelocytes; *n*, *n*, normoblasts; *p*, *p*, polynuclear neutrophiles; *r*, *r*, Reizungsformen (Türck) (cover-glass film stained with Ehrlich's "triacid" and drawn with camera lucida).

Nervousness, heredity, poor hygiene, and auto-intoxication from intestinal disorders have been alleged.

The blood is very pale, the number of red cells getting as low at times as 3,000,000, with from 40 to 30 per cent. of hemoglobin. The erythrocytes are very pale in the center, frequently show poikilocytosis, and may at times contain nuclei; normoblasts as a rule, megaloblasts are seldom present.

Changes in the leukocytes are unusual.

Leukemia is a disease of the blood-producing structures. It is characterized by a permanent increase in the leukocytes, other than the polymorphonuclear variety, and by lesions of the bone-marrow and lymphoid tissues.

The cause is unknown.

According to the type of leukocyte predominating in the blood leukemia may be *myelogenous*, *lymphatic*, or *mixed* when the two varieties are present.

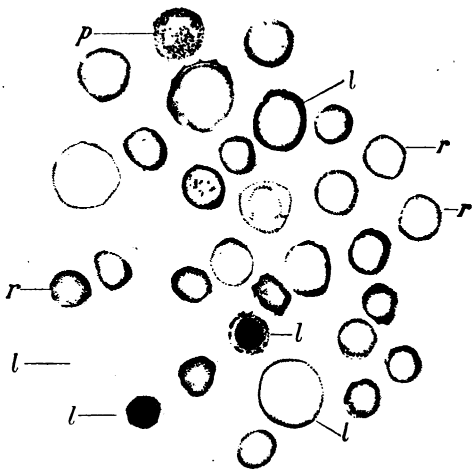

FIG. 113.—LYMPHATIC LEUKEMIA (Cabot).
l, l, l, l, l, Lymphocytes; *p*, polynuclear neutrophile; *r, r, r,* red cells.

The organs involved are the spleen, bone-marrow, and lymphatic nodes. There is marked infiltration of leukocytes and a hyperplasia of the lymphoid tissue. The spleen is much enlarged and shows grayish circumscribed areas. The marrow of the long bones loses its yellow color and becomes dark red. Numerous nucleated erythrocytes and eosinophiles are present.

The blood is pale and the specific gravity lowered. Co-

agulation is slow. The chief changes are in the leukocytes, which may number from 100,000 to 300,000 per cubic millimeter, or even up to 1,000,000.

The erythrocytes are reduced to about 3,000,000, the hemoglobin decreased and many contain nuclei. Is also some change in size and in shape.

In the *spleno-medullary* (*myelogenous*) type the myelocytes are present in great numbers, constituting from 20 to 60 per cent. of all leukocytes. The total number is about 450,000 per cubic millimeter. The main form is the large

FIG. 114.—HODGKIN'S DISEASE (Stengel).

Showing marked enlargement of the glands of the right axilla, with consequent dropsy of the arm; less marked involvement of the submaxillary and cervical lymph-glands.

mononuclear cell containing neutrophilic granules. The nucleus may be central and well staining or excentric and pale. This latter is seldom found in any condition other than leukemia. The neutrophile granules may be entirely lacking and the nuclei show hydropic degeneration.

Eosinophilic myelocytes may be found in large numbers, varying from 3000 to 100,000 per cubic millimeter.

Polymorphonuclear neutrophilic leukocytes decrease in number as the myelocytes increase. Degenerative changes in these cells are very common. They are more cohesive,

the nuclei show karyolysis or rhexis and hydropic degeneration.

Polynuclear eosinophiles are common. Lymphocytes are not very numerous in this form; constitute about 10 per cent. Mast cells are constantly increased in leukemia, but are difficult to find. At times may be as numerous as the eosinophiles.

In *lymphatic* leukemia the lymphocytes constitute from 80 to 90 per cent. of all leukocytes, which number about 100,000 or less per cubic millimeter. The lymphocytes are usually small, but sometimes the large mononuclear predominates, these latter being found more generally in acute cases and in children. Myelocytes, eosinophiles, polynuclear and mast cells are few. Nucleated erythrocytes very scarce.

In this form there is marked hyperplasia of the lymph-nodes, but the spleen seldom reaches the size that it does in the spleno-myelogenous type.

Changes in the number and variety of the leukocytes may vary greatly, either spontaneously or as a result of intercurrent disease.

Pseudoleukemia (Hodgkin's disease) is a condition in which there is a progressive increase in size of the lymph-nodes, particularly the cervical, without the blood changes present in leukemia. The characteristic and typical tissue change is a proliferation of the endothelial and reticular cells, with the formation of lymphoid and characteristic giant cells. Accompanying this is an increase in the connective tissue. Eosinophiles are usually present in great numbers.

The cause is not known. This condition seems to be more or less closely related to leukemia and lymphosarcoma.

Pseudoleukemia infantum (v. Jaksch).—This disease occurs in early childhood and is characterized by marked anemia, leukocytosis, and swelling of the spleen, liver, and lymph-nodes. There is, however, no leukocytic infiltration of the tissues.

CHAPTER XIX

DISEASES OF THE CIRCULATORY SYSTEM

DISEASES OF THE HEART

Congenital malformations may be the result of disturbances of development or of disease during fetal life.

There may be complete absence, as in acardiac monsters. Imperfect septa between the cavities is the most common defect. There may be no septum and a simple heart of two cavities, like that of a fish, is formed. If the ventricular septum is absent there are two auricles and one ventricle, the reptilian type. The auricular septum is often incompletely closed, giving rise to a patulous foramen ovale. The heart may be completely reversed, lying on the right side of the body with the aorta coming from the right ventricle and the other vessels correspondingly shifted. Is known as dextrocardia.

The arterial openings may be much smaller than normal, particularly the pulmonary. When the latter occurs there is marked cyanosis. If the stenosis is of a high grade the pulmonary circulation may be maintained by a persistent ductus arteriosus. Gives rise to hypertrophy of the right ventricle.

The valves may vary in number and also in length.

Diseases of the Pericardium.—May have *hydropericardium*, a collection of non-inflammatory transudate within the sac. *Hemopericardium*, when containing blood which gains entrance from rupture of the heart or of aneurysms of the great vessels. If in large amount it causes death by mechanically interfering with the contraction of the heart.

Pericarditis may be primary or secondary. In the

primary there is direct involvement of the pericardium by bacteria conveyed through the blood. In the *secondary* the condition results from the extension of inflammation from neighboring tissues.

FIG. 115.—ACUTE PERICARDITIS (Bramwell).

Primary pericarditis occurs in the course of such infectious diseases as acute rheumatism, scarlet fever, pneumonia, etc. The inflammation may vary greatly, and according to its

severity various forms of pericarditis are described. There is at first a dullness of the serous membrane with later a serofibrinous exudate. This may be slight or there may be 1000 to 2000 c.c. of fluid. The pericardium may become thickened, roughened, and covered by a coating of fibrin that may be quite marked. At the apex the fibrin is collected into strands, giving a villous appearance to the heart, the *cor villosum*. At the base of the heart, where the movements are more restricted, there is a "bread and butter" appearance.

As the serum is absorbed the fibrin may be replaced by connective-tissue adhesions until the pericardial sac is either partially or completely obliterated, *adhesive pericarditis*. As a result of this, marked hypertrophy may ensue and also some degeneration of the myocardium. Occasionally there is a deposit of lime salts in the organized tissue.

In the early stage there is microscopically a degeneration of the endothelium, which is covered by a layer of fibrin, and a round-cell infiltration of the subendothelial tissue.

Purulent pericarditis generally results from the extension of suppuration of some neighboring organ. It may start as a simple inflammation and later on give rise to a purulent exudate. The pericardial sac contains more or less purulent or seropurulent fluid. The myocardium is usually involved superficially; it becomes edematous, infiltrated with pus, and may undergo fatty degeneration; at times inflammation, myocarditis, may occur.

Tubercular pericarditis is commonly a part of a general miliary infection or it may result from an extension from a neighboring lesion of the pleura. The lesions found are similar to those occurring in tuberculosis in other parts.

Milk spots are irregular whitish areas found on the external surface of the heart. They probably result from constant pressure and are more accurately known as friction scleroses. There is a thickening of connective tissue below the endothelium.

Myocarditis or inflammation of the heart muscle is usually secondary to infectious conditions elsewhere, particularly in pericarditis. May be acute or chronic, diffuse or circumscribed.

In the *acute circumscribed* form numerous small metastatic abscesses are present. Beginning as minute points, generally in cases of malignant endocarditis, degeneration and necrosis may ensue, so that an abscess cavity the size of a cherry may develop. This may perforate into the cavities of the heart, into the pericardium, or may form a cardiac aneurysm. The abscess may lose its liquid contents, become encapsulated or infiltrated with lime salts.

FIG. 116.—CHRONIC FIBRINOUS MYOCARDITIS. × 80 (Dürck).
1, Heart musculature; 2, long connective-tissue fibers between the muscle-bundles, containing but very few nuclei and blood-vessels.

In the *acute diffuse* variety, as seen in diphtheria and scarlet fever, there is a diffuse round-cell infiltration between the muscle fibers with proliferation of the connective-tissue cells as well. The muscle fibers become granular, opaque, and the striations indistinct. They may undergo Zenker's hyaline degeneration. If the patient recovers scar tissue may form.

The heart is soft and friable, and usually lighter in color than is normal, and the fibers are easily separated. Dilatation of the left ventricle is often present.

In *chronic fibrous myocarditis* the lesions may be diffuse or localized. It may be the result of a former acute diffuse myocarditis or it may be secondary to diseases of the coronary arteries or to disturbances of their circulation. In the muscle are seen spots or streaks of sclerotic tissue. Microscopically greater or less amounts of connective tissue are found separating the fibers which frequently undergo a fatty degeneration as a result of pressure and thus give rise to irregular yellowish areas.

Some of the sclerotic portions found along branches of the coronary artery probably represent healed infarcts.

Fatty metamorphosis is often found in toxic and infectious diseases. Is usually irregular in its distribution, forming areas of yellowish tissue, easily distinguished beneath the endocardium. In the fibers are found fat granules; the striations disappear and the nuclei may show degenerative processes.

Brown atrophy is a condition in which the heart is reduced in size and is brownish-red in color. Is found in old age and in chronic cachexias. Within the muscle fiber at the ends of the nuclei are found numerous minute brownish granules (Fig. 12).

By **endocarditis** is indicated an inflammatory condition of the serous membrane lining the heart. Is most common upon the valves, although the endocardium of the cavities may be involved. It may be divided into the acute and the chronic; the acute being subdivided into the *verrucose* and the *ulcerative*.

Acute endocarditis is a secondary condition occurring in the course of an infectious disease as a result of the action of bacteria. It is characterized by the formation of cauliflower growths upon the valves or by ulceration of the leaflets.

It is found particularly in acute articular rheumatism, in pneumonia, scarlet fever, puerperal sepsis, and gonorrhea. The organisms most commonly found have been the staphy-

lococcus, streptococcus, and diplococcus pneumoniæ, also the gonococcus.

The most common seats are the mitral valve, then the aortic and pulmonary valves. In fetal endocarditis the right side of the heart is more frequently involved. Instead

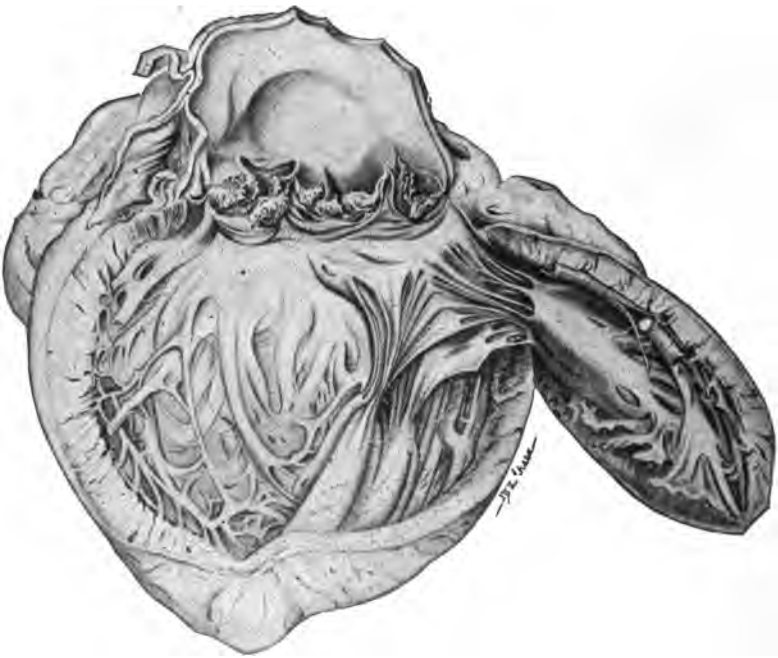

FIG. 117.—CHRONIC VERRUCOSE ENDOCARDITIS OF THE AORTIC VALVES, SHOWING THE WARTY PROJECTIONS FROM THEIR EDGES. THE VALVES ARE AT THE SAME TIME THICKENED AND STIFFENED BY SCLEROTIC CHANGES (McFarland).

of the edge the lesion first occurs on the line of closure. The endocardium becomes opaque and small, irregular nodules appear (*verrucose endocarditis*). These elevations consist of layers of fibrin, beneath which is the endocardium, show-

ing desquamation of the endothelium with also round-cell infiltration and proliferation of the fixed connective-tissue cells. In the masses of fibrin will be found blood plates, leukocytes, and frequently bacteria.

The process may terminate by a degeneration of the vegetations with the formation of scar tissue and subsequent thickening and contraction. There may also be marked calcareous infiltration.

If the condition continues there may be destruction of the valve, *ulcerative endocarditis.* In this there is a superficial necrosis of the valve with a deposit of fibrin upon the ulcerated surface. As the lesion progresses the leaflet may become weakened and distended by the blood-pressure, forming an aneurysm of the valve. Perforation may occur and portions of the leaflet, or of the fibrin mass may be set free in the blood as emboli. These generally contain bacteria, and, lodging in the brain, kidney, and spleen, will give rise to metastatic abscesses.

Either of these two varieties may terminate in the chronic form.

In *chronic* or *sclerotic* endocarditis there is an overgrowth of fibrous tissue, usually with calcification, causing a distortion of the valves. The leaflets become thickened, less elastic, rigid and hard, and frequently shortened. As a result the lumen of the orifice may be decreased and give rise to obstruction to the flow of blood (*stenosis*). On account of the lack of elasticity the valves are no longer able to completely close the orifice, so there is a backflow of blood (*regurgitation*).

There is also frequently present a shortening and thickening of the chordæ tendineæ, which on account of preventing the valves from closing gives rise to regurgitation.

This form of endocarditis may be a sequel to the acute varieties or it may gradually develop independently of such conditions.

There may also be bits of tissue or fibrin broken off with resulting embolism.

As a result of the disturbances of the circulation which call for increased effort, there is hypertrophy of the heart with subsequent dilatation.

CARDIAC HYPERTROPHY

In this condition there is an increase in both the number and size of the muscle fibers. It may be the result of either *outside* interference to the heart's action, as in adhesive

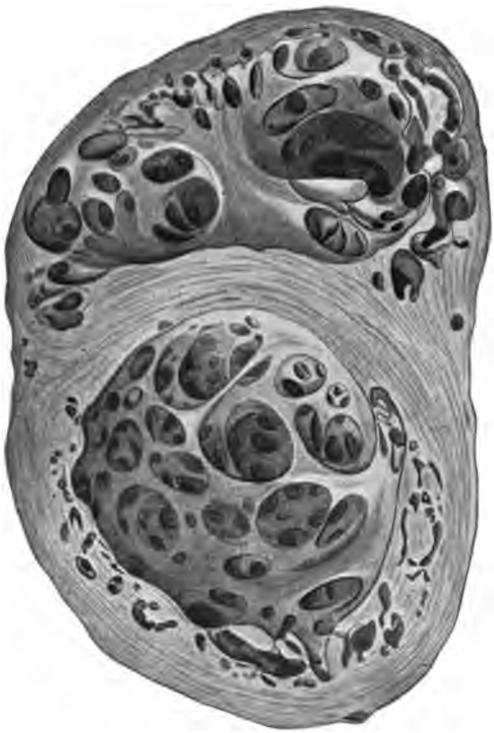

FIG. 118.—HYPERTROPHY AND DILATATION OF THE HEART (Bollinger).

pericarditis; or *inside* resistance, as occasioned by valvular lesions. It also occurs when there is increased resistance to the flow of blood, as is found in arteriosclerosis.

Hypertrophy will, however, occur only when the heart is primarily able to overcome the obstacle. If unable to do so,

there will be relaxation, dilatation. As a rule, one chamber of the heart is chiefly involved, but it is unusual not to find other chambers more or less affected.

When the heart enlarges sufficiently to overcome its obstructions and the circulation is carried on without any apparent trouble, the condition is known as *compensatory hypertrophy*. This may continue for a long time, but there finally comes a moment when the heart is no longer able to do its work. The symptoms then of failure of compensation make their appearance.

FIG. 119.—ATHEROMA OF THE AORTA (Bollinger).

According to the location of the obstacle different cavities of the heart are involved. In the most common valvular lesion, mitral regurgitation, there is a hypertrophy of the left ventricle. In lesions of the aortic valve the greatest enlargement may occur, giving rise to the "cor bovinum." Any interference with the systemic circulation will give rise to this condition.

Enlargement of the right ventricle arises from interference with the circulation within the lung, as in emphysema.

The hypertrophy resulting from valvular lesions is due to the cavity containing a greater amount of blood than is normal, whether stenosis or insufficiency or both be present.

If there is stenosis, the entire charge of blood is not pushed forward before the heart enters into diastole and receives another supply from the auricle. If there is regurgitation the ventricle during its diastole receives blood both from the auricular and from the distal sides. In either case the heart must increase its muscular power before the circulation can be properly carried on.

The hypertrophied heart may weigh as much as 1000 or 1500 grm. in extreme conditions, more commonly from 700 to 800 grm.

Three forms of cardiac hypertrophy may be described:

I. *Simple hypertrophy*, in which there is an increase in the thickness of the muscular wall without any diminution in the capacity of the cavity.

II. *Excentric*, in which there is increase in the size of the cavity and in the thickness of the walls.

III. *Concentric*, in which there is thickening of the wall with diminution in the cavity. This is probably a pure port-mortem finding, being an arrest in systole of a hypertrophied heart.

CARDIAC DILATATION

This may be either *acute*, as a result of severe muscular exertion, or *chronic*, following hypertrophy. Consequently the walls may be either abnormally thin or correspondingly thick.

Dilatation is due either to a *weakening of the cardiac walls*, following interferences with nutrition, or to an *increase in the cardiac blood-pressure*.

The failure of nutrition is due to interference with the coronary arteries. In this the heart walls become soft and flabby.

DISEASES OF THE ARTERIES

Endarteritis, or inflammation of the artery, usually results from the presence of foreign bodies, either infectious or sterile, within the vessel. It may be caused by organisms gaining entrance into the vasa vasorum. The intima is

first involved; it becomes roughened, the endothelial cells become loosened, and there is usually an infiltration of round cells. The vasa vasorum are involved and the inflammatory process may extend to the media or the adventitia, and as a result a thrombus generally forms within the lumen.

Periarteritis is an inflammatory condition around an artery, usually arising from injuries from without, or sometimes by extension from within. There is an infiltration of

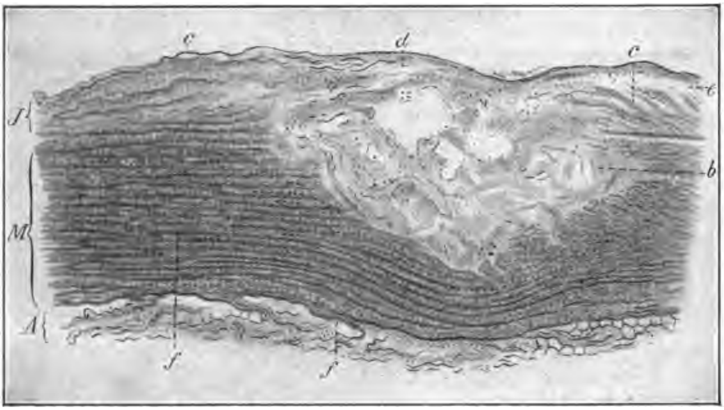

FIG. 120.—AN ATHEROMATOUS PATCH IN THE ABDOMINAL AORTA WHICH HAS NOT YET BROKEN THROUGH (Dmitrijeff).

J, Intima; *M*, media; *A*, adventitia; *b*, atheromatous necrotic focus in the intima and media; *c*, elastic fibers of the intima; *d*, elastic fibers which have persisted between the necrotic focus and the endothelial layer; *e*, thickened endothelium; *f*, infiltration of the media with small cells.

the adventitia, which becomes swollen and edematous. The media and intima become involved, there is desquamation of the endothelium with the formation of thrombi.

Arteriosclerosis, arterio-capillary fibrosis, or chronic arteritis, is a condition characterized by an increase in connective-tissue formation accompanied by degenerative changes. These may be circumscribed or diffuse. The fibrous formation occurs chiefly in the outer coats and is referred to as

sclerosis, the degenerative processes involve the intima and are spoken of as *atheroma*.

The large vessels such as the aorta are most commonly affected, but the arteries at the base of the brain and the splenic artery are frequently involved.

In the circumscribed form, *arteriosclerosis nodosa*, numerous small oval or round yellowish-white areas are visible. These are but slightly elevated and vary in their consistency according to the structure. If there is much connective tissue, they may be very firm; if degenerative changes have occurred, they will be soft.

As as result of the presence of these areas the elasticity of the vessel is interfered with, nutrition suffers, and connective tissue forms. Beneath the intima there will be found areas of softened semifluid substance, *atheromatous cysts*, covered by an imperfect layer of endothelium. This covering may break off, allow the contents to escape, leaving a cavity known as an *atheromatous ulcer*. The material found within these so-called cysts is composed of tissue that has undergone a fatty degeneration. Microscopically yellowish granules and droplets of fat as well as crystals of fatty acids are present. Instead of escaping, the cystic contents may become markedly infiltrated with lime, thus forming *atheromatous plates*.

Whenever an atheromatous ulcer has formed, the wall of the vessel at that point may be thinner and less elastic than normal. As the elasticity of the vessels is decreased there is consequent increase in blood-pressure with hypertrophy of the left ventricle. With the increased pressure there occur dilatations of the vessel at its weakened points, with the formation of aneurysms.

In the smaller vessels, particularly of the brain, rupture or apoplexy quite frequently occurs.

In *diffuse arteritis* or *arterio-capillary fibrosis* the smaller arteries and capillaries are the seat of fibrous tissue formation. Resulting from this, there may be more or less lessening in the lumen of the vessel, *endarteritis deformans*.

If the lumen is completely occluded, is known as *endar-*

teritis obliterans. In both cases there will be interference with the supply of nutrition and degenerative changes, chiefly hyaline, of varying degree consequent.

These lesions are very common in both syphilis and tuberculosis. In the first there is a cellular proliferation beginning in the adventitia but ultimately involving the intima.

Aneurysm.—An *aneurysm* is a circumscribed dilatation of an artery. It may be (1) *true* or (2) *false*, according to

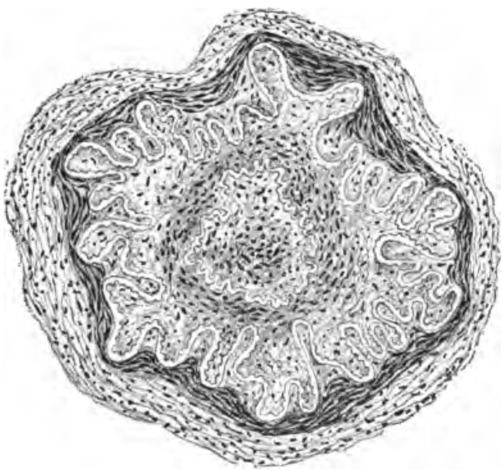

FIG. 121.—ENDARTERITIS PRODUCTIVA (Dürck).

whether (1) all the arterial coats are involved or (2) whether there has been a rupture of one or more of the coats.

Aneurysms may be single or multiple, and may vary greatly in size. They result either from injury or disease of the vessel or from increased arterial blood-pressure.

They are classified according to their form. They may be:

1. *Saccular,* in which case there is a hemispherical dilation extending from one side of the artery.

2. *Fusiform,* a cylindric dilatation extending for some distance along the artery.

3. *Dissecting.* In this variety the blood passes through an

FIG. 122.—ANEURYSM OF THE ARCH OF THE AORTA (Bollinger).

opening in the diseased intima and makes its way between it and the media, or between the media and adventitia. Occasionally the blood may re-enter the lumen through a lesion further along in the course of the vessel. Is most common in the large arteries.

In the brain there is quite frequently found a condition known as multiple miliary aneurysms. In the course of the small vessels, particularly branches of the lenticulo-striate, numerous very small dilatations may be found. They are probably the result of degenerative changes in the media.

After an aneurysm has once been formed it may be rendered harmless by means of the deposition of layers of fibrin within the cavity. This may go on till there is complete obliteration, this, however, does not frequently occur. Although an aneurysm is a soft structure there may be extreme destruction of surrounding tissues, particularly of bone. The pressure exerted by the aneurysm shuts off the periosteal blood-supply and more or less erosion of the bone follows.

Ultimately rupture of the sac generally occurs. The walls have become so thinned and weakened that they are no longer able to resist the pressure. Rupture commonly takes place when there has been some unusual muscular exertion. It may occur, though, when the individual is quiescent.

DISEASES OF THE VEINS

Thrombosis has already been discussed under that general heading.

Phlebitis, inflammation of the veins, may follow inflammatory conditions around the vessel, from traumatism, or it may arise from conditions within, by infection from microorganisms circulating in the blood. It may be an *acute purulent* form in which there is first an infiltration of round cells, then rapidly of pus cells. This condition follows along the vessel, forming abscesses and thrombi. The formation of the latter depends upon the loss of integrity of the intima. The thrombi act as plugs so as to prevent as well as possible the entrance of the invading organisms into the blood, but they may break down and send forth innumerable particles of infecting material.

Chronic phlebitis, or *phlebosclerosis*, is a condition similar to arteriosclerosis, but is much less common. In it the sclerotic processes predominate, the atheromatous being less marked.

Varicose veins are ones in which dilatation has occurred. This may take place in the neighborhood of a valve, and by rendering it incompetent the blood-pressure is increased. In this way the greater part of a vein may be distended. If the vessel has become longer than normal it will naturally be more tortuous (cirsoid). In this form the various loops may come in contact, and at that point undergoing atrophy of their walls communications will be established; these are known as *varices*, or *varix*. Such portions resemble cavernous or erectile tissue.

In the dilated portions thrombi may form or a periphlebitis with the formation of dense connective tissue take place. Phleboliths are also quite common.

Interference with the venous return seldom leads to as severe results as corresponding lesions in the arteries. This being due to the readiness with which collateral circulation can be established. Varicose veins are most common in the lower extremities. There is generally edema present, and if a skin surface is involved extensive ulcerations may form. These ulcers heal with difficulty on account of the poor nutrition. Another result of venous congestion is the formation of dense connective tissue.

The varicose condition is the result of disease of the vessel wall or of increased venous pressure, brought about by interference with the return flow. This is well seen in the long veins of the lower extremity.

Special names have been given to varicose conditions of certain veins. Dilatation of the spermatic veins is known as *varicocele;* of the hemorrhoidals, as *hemorrhoids.*

LYMPHATICS

Inflammation of the lymph-vessels, *lymphangitis*, is nearly always secondary to bacterial infection. It frequently follows superficial injuries, particularly those received in the making of autopsies. It appears clinically as reddish streaks extending from the point of infection. The inflammation may go so far as to involve distant lymph-nodes, which become swollen, tender, and sometimes suppurate.

The lymph-vessels may become dilated, *lymphangiectasis.* Is usually due to obstruction by parasites. Is found in elephantiasis.

If there is any defect in the wall of the vessel the lymph may escape into an adjoining cavity or upon the surface of the body. When it enters the abdominal cavity chylous ascites ensues.

Tuberculosis of the lymphatics, particularly when there is tuberculosis of the serous membranes, is common. The vessels appear as grayish lines.

Syphilis commonly involves the lymph-nodes in all its stages.

CHAPTER XX

DISEASES OF THE RESPIRATORY SYSTEM

DISEASES OF THE NOSE

Malformations of varying degrees of severity, from complete absence to slight cleft lip, may exist. There may be no external abnormality, but the floor of the nasal cavity may be lacking, the septum deviated, or there may be complete obstruction to one or both nostrils by bony growths.

Rhinitis or **coryza** is an inflammatory condition of the mucous membrane of the nose. It may be acute or chronic and be caused by direct or indirect influences.

The *acute* form is generally attributed to cold, but may be brought about by exposure to the inhalation of various irritating bodies, as pollen of flowers or the fumes of various chemicals, by the action of micro-organisms, or by vasomotor disturbances.

There is first a condition of hyperemia and dryness of the nasal mucosa, which is soon followed by a discharge that is serous, seromucous, or mucopurulent in character. This may cause excoriation of the tissues that it comes in contact with. In the discharge are found epithelial cells and leukocytes as well as bacteria.

Chronic rhinitis usually follows repeated attacks of the acute form, but may be due to some abnormality of the nose itself. It may be of two forms, the hypertrophic and the atrophic.

In the *hypertrophic* variety there is congestion of the veins with thickening and swelling of the mucosa. The mucous glands increase in size, there is a thick, viscid secretion, and the nasal passages are much obstructed, particularly by enlargement of the lower turbinated bones. There is also a hyperplasia of the connective tissue.

The *atrophic* form may follow in the course of the hypertrophic. The hyperplastic fibrous tissue shrinks, the epithelium of the mucosa and the glands are destroyed, and there is a secretion of a yellowish purulent matter. This latter has an extremely disagreeable odor; the condition is termed ozena. The bony septum may even be destroyed. In the discharge saprophytic organisms as well as others may be found.

Diphtheria may involve the nasal mucosa primarily, but usually is secondary to the pharyngeal form. In it there is a pseudo-membrane formed and the organism of diphtheria can be found.

Syphilis generally occurs in the form of a coryza that does not differ from that arising from other causes. In the later stages ulceration with necrosis of the bones may occur. Gumma situated within the periosteum or perichondrium may form. This is often followed by destruction with the sinking in of the bridge of the nose.

Tuberculosis may give rise to ulceration with subsequent necrosis. In the discharges the tubercle bacilli can be demonstrated.

Leprosy is said to be first demonstrable in discharges coming from ulcerations of the nose.

Glanders may be conveyed from a diseased horse to the nasal mucosa of man and give rise to nodules or farcy buds.

Tumors.—The most common form is that known as a *polyp*. Polyps are composed of fibrous tissue, that is generally myxomatous, and a covering of mucous membrane. These growths may be mucous, adenomatous, cystic, or telangiectatic.

Various forms of connective-tissue tumors, as the fibroma, chondroma, osteoma, and sarcoma, occur. The *fibroma* may give rise to severe hemorrhage if it is highly vascular. The *sarcoma* is the most common malignant tumor. It may arise from the septum, but more frequently it extends from the antrum.

Carcinoma is not so common, but epitheliomata may develop at the junction of the skin and mucous membrane.

Chondritis and *perichondritis* are inflammations of the cartilages of the larynx secondary to ulcerations of adjoining tissues. The cartilages, being very poorly supplied with blood, have their nutrition interfered with by the inflammatory conditions and degenerative changes ensue. In old age the cartilages may undergo calcification.

DISEASES OF THE LARYNX

Malformations of the larynx are neither numerous nor specially important. The parts may be unsymmetric or there may be a fistula resulting from the imperfect closing of a branchial cleft.

Acute laryngitis or inflammation of the larynx results from exposure to cold, from inhalation of irritating vapors and substances, or is due to infections secondary to disease of the mouth, pharynx, or lung. It begins with a congestion and swelling of the mucosa. This is followed by increased secretion with disturbances of the voice due to involvement of the vocal cords. There is a round-cell infiltration of the tissue with sometimes ulceration, in the healing of which scar tissue forms.

Chronic laryngitis often follows acute attacks or it may develop independently. In it there is dilatation of the vessels and hypertrophy of all the portions of the mucosa. There is a slight thick secretion and the membrane looks distinctly granular on account of the swollen glands, *granular laryngitis*. Is generally found in singers and lecturers.

Edema may occur slowly, as in passive congestion and in chronic inflammations, or it may take place very rapidly (*acute edema of the glottis*) as a result of some sudden and severe inflammatory process, as from the inhalation of steam, gases, or the action of irritating substances. In it there is a serous infiltration of the arytenoid cartilages and the aryteno-epiglottic folds. These swollen tissues meet in the middle and more or less completely obstruct the passage of air into the lungs.

In **diphtheria** of the larynx, which may be primary or secondary to that of the pharynx, there is an acute inflamma-

tory process with marked exudation. This contains much fibrin and, undergoing coagulation, forms a pseudo-membrane. In it, besides the fibrin, are found pus cells, desquamated epithelium, bacteria, and sometimes a few red cells. This membrane is grayish in color, tough, and when removed leaves a raw bleeding surface.

It may occur as an extensive layer over the larynx or in isolated areas. It may be removed, but reproduces very rapidly.

Although membrane is more commonly caused by the diphtheria bacillus, it may result from streptococci or from the action of irritating vapors.

Tuberculosis of the larynx is quite common as a primary lesion, usually being an infection on top of a chronic inflammation. It generally appears in the form of scattered miliary tubercles which frequently break down and ulcerate. This occurs rapidly on the vocal cords. The lesions are most common about the posterior commissure, the arytenoid cartilages, and the true vocal cords, seldom on the epiglottis.

The ulceration may be very destructive, involving the submucosa and even the cartilages, causing inflammation and necrosis of them.

The larynx may be the seat of the slowly spreading form of tuberculosis known as lupus.

Syphilis may be either of a mild or a very severe type, the commonest form being a simple catarrhal laryngitis with infiltration of the mucosa and submucosa. Gumma may form, break down, and give rise to extensive ulceration, with perichondritis and necrosis. As the healing processes go on, large amounts of fibrous connective tissue are formed. These undergo contraction with frequently marked deformity.

Leprosy gives rise to nodular lesions, quite similar to what may be found in syphilis. They break down, ulcerate, and in healing form large scars.

Glanders is rarely found. In it there is a cellular infiltration with the formation of suppurating ulcers.

Foreign bodies of various sorts may gain entrance and become lodged in the larynx.

Tumors.—The most common tumors are the *papillomata.* They vary greatly in size and shape and the greater number are of inflammatory origin. They consist of a more or less dense framework of fibrous tissue covered by a layer of epithelium. These growths may be quite flat and but little raised above the surrounding surface, or they may be distinctly polypoid. The fibrous tissue may show mucous changes, and the glandular structures be distended with secretion, so as to form cyst-like growths.

Small *fibromata* are sometimes found. *Adenomata* are rare.

Malignant tumors may occur; of these, the *sarcoma* is very rare. When present, it does not involve the cervical lymph-nodes. The *epithelioma* is more common and may arise from either the vocal cords and ventricles or from the arytenoid folds and the epithelium covering the cartilages.

DISEASES OF THE TRACHEA AND BRONCHI

Malformations of the trachea usually consist of a fistulous opening, the result of failure of closure of the third or fourth branchial cleft. Generally appear along the anterior border of the sternomastoid, a little above the clavicle.

The trachea is the seat of inflammatory processes secondary to those in the neighboring portions of the respiratory system, the larynx, and the bronchi.

Bronchitis may be either acute or chronic. In the acute variety the mucosa becomes congested with swelling, and in the beginning secretion is decreased. There is soon an increased exudation, at first thin and with but few pus cells, but soon becoming thick and tenacious and containing more cells.

If there is much expectoration of a serous type the condition is known as *bronchorrhea serosa;* if purulent in character, *broncho-blennorrhea.*

The cause of bronchitis is not definitely known; it may be infectious in its nature, but it commonly follows exposure to cold.

Chronic bronchitis may follow repeated acute attacks or accompany various chronic diseases of the lung, particu-

larly in those in which there are marked circulatory disturbances. The mucosa is much congested, the secretion may be scant or plentiful, and there may be distinct projections on the walls. Instead of proliferative changes there may be atrophy with weakening of the bronchial walls and dilatations.

Fibrinous bronchitis is a condition in which a small area of the terminal bronchi and bronchioles are involved. It is marked by the expectoration of a dense yellowish-white substance moulded in the shape of the air-passages from which it came. The larger stalk is usually hollow, the smaller branches being solid and the walls commonly laminated. Although resembling fibrin it does not give the characteristic reaction and is evidently inspissated mucous. In the meshes of the bronchial cast are leukocytes, broken-down epithelium, and Charcot-Leyden crystals such as are found in asthma. Curschmann's spirals are also found. These are collections of fine fibrils twisted like a corkscrew. They are present at the end of the smallest branches of the cast.

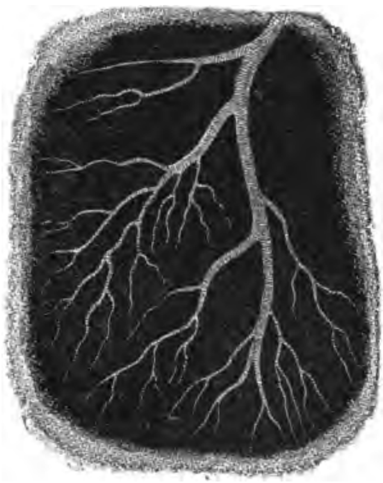

FIG. 123.—LARGE BRONCHIAL COAGULUM; CHRONIC FIBRINOUS BRONCHITIS (Vierordt).

In diphtheria and in croupous pneumonia there may be the formation of a true fibrinous exudate. The mucosa of the bronchi is reddened and is more or less completely covered by a pseudo-membrane.

Bronchiectasis, or dilatation of a bronchus, may follow

chronic bronchitis in which there has been atrophy and weakening of the bronchial wall, or it may be due to an increase in the air-pressure. The medium-sized bronchi are the ones most frequently involved. The enlargements are usually saccular, but may be fusiform or cylindric. There may also be several in the course of a single bronchus. The walls may appear of normal thickness, but this is due to fibrous tissue formation, as the normal tissues are atrophic.

In fibroid phthisis the contraction of the new formed fibrous tissue may drag upon the bronchi and cause them to dilate.

As the walls become weakened, secretions in large amounts may be retained and by their weight cause extensive bronchiectasis. The various dilatations may, on account of atrophy of the intervening tissues, communicate. They may be filled with secretion, with cyst formation resulting. This material may undergo decomposition with subsequent gangrene or it may dry up.

Obstruction of a bronchus may be the result of inflammatory changes within the wall, of tumors or foreign bodies inside, or of pressure from the outside.

Foreign bodies more commonly lodge in the right bronchus, and may cause ulceration and pneumonia or gangrene of the lung.

Tumors.—Primary growths are uncommon, but secondary tumors are more frequent, particularly carcinomata.

DISEASES OF THE LUNGS

Circulatory Disturbances

Anemia of the lung seldom occurs. Is due to pressure causing vascular obstruction.

Acute hyperemia or congestion may be caused by the inhalation of irritating gases or it may be collateral, due to obstruction in some other part of the lung. It is also the first stage in inflammations of the lung. The organ is dark red in color; on section blood escapes from the cut surface. The tissue will float in water.

Chronic or passive hyperemia is generally due to obstruction of the pulmonary veins, and is associated with disease of the aortic and mitral valves and a weakened condition of the circulation. The dependent portions alone may be involved —*hypostatic congestion.*

The lung in passive hyperemia is dark red in color, firm, and crepitation is less than normal. From a cut surface there escapes on pressure a frothy purplish fluid. Resulting from the congestion, there is frequently proliferation of the fibrous connective tissue, giving rise to *cyanotic* induration of the lung. There is desquamation of the epithelium which contains pigment that has formed through the destruction of red cells. This form of hyperemia is frequently seen post mortem.

In *edema* of the lung there is an escape of serous fluid into the bronchi and air-vesicles. Is generally found as a result of chronic congestion following heart and kidney disease, but may follow the inhalation of very hot or very cold air. Is also found as a terminal affection in many diseases. The lung may be either pale or dark, according to the amount of congestion present. Is heavy and boggy, but crepitates, and from the cut surface a thin, frothy serum escapes in large quantities.

Hemorrhage from the lung, or *hemoptysis*, occurs in many conditions—trauma, embolism, etc.—but is most common in phthisis, particularly in the later stages when ulceration has taken place. The blood may be expectorated or part of it may enter portions of the lung. These areas do not contain air, are dark in color, and resemble splenic tissue.

Hemorrhagic infarction is merely a localized hemorrhagic area following obstruction of the arteries by emboli. The area is usually just beneath the pleura with its base circumscribed and directed outward, the apex directed toward the hilum; is dark red, almost black in color, dense and airless. The air-spaces are filled with erythrocytes and some fibrin. Infarcts may be small or large, single or multiple. If infection does not take place the tissues may regain their normal condition. Usually there is degeneration with subsequent cicatrization, an irregular depressed scar resulting.

Atelectasis or collapse of the lung may be either congenital or acquired. The *congenital* form occurs in newborn babies who have never breathed, either on account of an obstruction to a bronchus or from lack of strength. The entire lung or portions only may be involved. Obstruction of the upper air-passages by meconium or amniotic fluid will cause atelectasis.

The *acquired* form develops after expansion has once taken place, and may result from pressure from the outside, as in pleuritic effusions, neoplasms, etc., or it may follow obstruction of a bronchus with absorption of the contained air, the vesicles then collapsing. The involved area varies in color, according to the amount of blood present, from a pale red to a dark brownish color. The tissue is dense, dry, tough, does not contain air, and will not crepitate; will sink when placed in water. If there is much congestion, the tissue looks like meat and the condition is termed *carnification*. If the atelectasis has existed for some time, there is proliferation of fibrous connective tissue, giving rise to an appearance resembling the spleen, known as *splenization*. Inflammation, with fibrosis and the deposit of lime salts, may occur in the involved area.

Emphysema is a condition of overdistention of the air-cells with an increased amount of air present in the lung. It is due either to a loss of elasticity of the air-cells, to an increase in the air-pressure, or to both. In *interstitial* emphysema there is rupture of the air-vesicles with the entrance of air into the interlobular tissue of the lung, small bubbles appearing beneath the pleura.

Acute vesicular emphysema results from forced inspiration. In it there is merely over-distention of the vesicles without structural alterations.

In *chronic vesicular* or *substantial* emphysema there is extensive and permanent dilatation of the vesicles. Is generally found in those who suffer from chronic bronchitis and in glass-blowers or players of wind-instruments, the important factor being obstruction to the expiration. The lung is much increased in size, pale in color, and feels like cotton.

The loss of color is due in great measure to an actual disappearance of pigment. The edges are rounded, particularly anteriorly and at the apex. The vesicles may be so enlarged as to be visible to the naked eye.

Microscopically the vesicles are seen to be greatly enlarged,

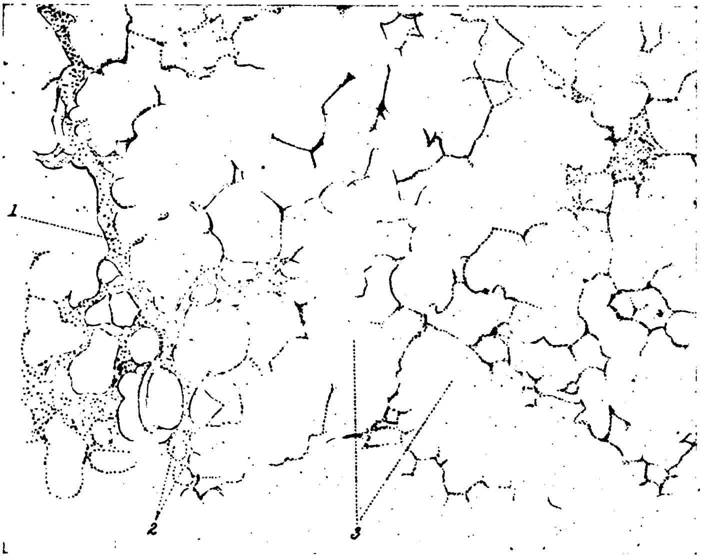

FIG. 124.—EMPHYSEMA OF THE LUNG. 40 × (Dürck).

Greatly dilated alveolar spaces, extraordinarily thin alveolar septa, deficient in cells and torn at many places so that the several alveoli communicate with one another. 1, Interlobular septum; 2, contiguous but normal alveoli; 3, dilated and confluent alveoli.

and the walls much thinned. In many places rupture of the walls may be seen with the formation of one large alveolus from several smaller ones. As the walls are stretched the capillaries become narrowed and may finally be completely obliterated. As a result nutrition is interfered with and degeneration and atrophy follow.

In this form of emphysema the chest is barrel shaped. The pulmonary circulation being interfered with, enlargement of the right heart with general venous congestion ensues.

Senile emphysema is that occurring in old age from atrophy of the intervesicular septa. *Vicarious* emphysema is that found in one part of the lung as a result of obstruction in some other portion.

Pneumonia

Pneumonia, or *inflammation* of the lungs, can be divided into various forms according to the nature of the inflammatory exudate, to the mode of entrance of the etiologic material, and to the portion of the lung involved. *Fibrinous* pneumonia when the exudate into the air-sacs and bronchioles is rich in fibrin; *catarrhal* when the exudate contains an albuminous fluid in which are desquamated epithelial cells and erythrocytes; *purulent* when pus cells are numerous; *caseous* when there is cheesy necrosis, and *fibrous* when there is extensive fibrous connective-tissue formation.

It may be *lobar* or *lobular*.

Aërogenic when the infecting substance is conveyed by the air through the bronchi; *hematogenic* when carried by the blood; *lymphogenic*, by the lymphatics; *pleurogenic*, by extension from the pleura.

Inspiration pneumonia, when a large amount of infecting substance gains entrance by the bronchi.

Hypostatic, when the blood, on account of weakened circulatory efforts, settles in the dependent portions of the lung and consolidation takes place.

Pneumonias may also be *acute* or *chronic*.

Croupous, fibrinous, or **lobar pneumonia** is an acute infectious disease, generally caused by the diplococcus of Fränkel. It usually involves one or more lobes, an entire lung, or rarely both lungs. It is characterized by an exudation, rich in fibrin, into the air-spaces and bronchioles.

Morbid Anatomy.—The lower lobe of the right lung is most frequently first involved, then the lower left, the apices seldom primarily. An entire lobe is generally involved.

The course of the disease can be best studied by arbitrarily dividing it into three stages—that of *congestion*, of *red* and *gray hepatization*, and of *resolution*. It must be remembered that all of these conditions may be present in one lung at the same moment.

Stage of Congestion.—The lung is actively hyperemic, dark red in color, enlarged, and firm. Is very friable and contains but little air. The air-vesicles are filled with fluid in

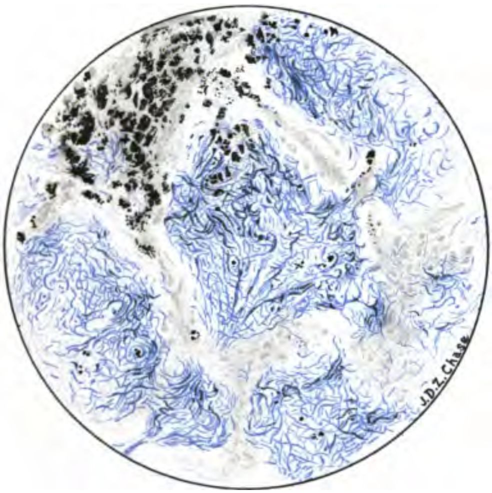

FIG. 125.—CROUPOUS OR FIBRINOUS PNEUMONIA, STAGE OF RED HEPATIZATION; STAINED BY WEIGERT'S METHOD TO SHOW THE FIBRIN ONLY. × 180 (McFarland).

The blue threads filling the air-cells consist of fibrin-filaments.

which are found numerous red cells, a few leukocytes and epithelial cells. The capillaries are greatly distended.

Stage of Red Hepatization.—In this the exudate has undergone coagulation and there is complete absence of air from the involved area. The lung is solid and resembles the liver in consistency. Is swollen, dark red in color, and pits on pressure. From the cut surface, which is quite dry, there

project minute plug-like bodies formed of fibrin, which give a granular appearance to the tissue. They are formed by the coagulated exudate in the alveoli being pushed outward by the contraction of the elastic fibers. The pleura generally shows some fibrinous exudate. Microscopically the air-vesicles are seen to be filled with red cells entangled in a network of fibrin; leukocytes and epithelial cells are also present. The capillaries are less prominent. The diseased tissue will sink when placed in water.

Stage of Gray Hepatization.—With the beginning of this stage recovery is indicated. The lung loses its red color and becomes gray or yellowish. This is shown microscopically to be due to changes taking place within the alveoli. The blood-supply being interfered with, the exudate undergoes fatty degeneration. The erythrocytes have broken down, the fibrin has disappeared, and leukocytes are now present in great numbers. The exudate no longer closely adheres to the walls, but leaves space for the entrance of air.

Stage of Resolution.—The broken-down exudate is removed by absorption and by expectoration. The leukocytes also carry off much of the debris. The lung becomes more moist, is less solid, and crepitation returns. The epithelium of the alveoli and bronchioles proliferates and the lung returns to the normal. There is sometimes a delay in the return of the normal elasticity of the alveolar walls.

Instead of the lung returning to the normal various complications may arise. Infection by pyogenic bacteria may take place, with abscess-formation. Gangrene may also follow, particularly if the circulation is weak. Resolution may be delayed and proliferation of connective tissue occur, giving rise to *fibrous pneumonia.* Microscopically there is seen an extensive cellular infiltration and proliferation. The septa become much thickened and masses of connective tissue extend into the air-vesicles. In alcoholics there is a marked hemorrhagic tendency.

There may be serious conditions associated with lobar pneumonia. The uninvolved portions may be emphysematous and congested, and sometimes edema develops. The

infecting organism may gain entrance into the blood and cause inflammations of the serous membranes, particularly endocarditis and pericarditis. Cardiac disturbances may occur, probably due to the action of toxins. There is also usually some involvement of the kidneys. Leukocytosis is generally marked. Tuberculosis may follow the pneumonia.

The symptoms in this disease would seem to depend more upon a toxic condition than upon mechanical obstruction to breathing by the filling of the alveoli. This would seem to be shown by the fact that on the fall of temperature, the crisis, the alarming objective symptoms subside. Yet a physical examination made at that time shows no changes in the lung itself.

Death may result from the action of the toxins, from overburdening of the heart, or from some of the associated conditions, as edema or gangrene.

Catarrhal pneumonia or bronchopneumonia is an inflammatory condition of localized areas of the lung resulting from inflammation of the terminal bronchioles. Is also known as *lobular* pneumonia, on account of involving lobules of the lung. Occurs generally in young children and old people. It is due in the majority of cases to infection. Is most common as a sequel to the infectious fevers that are accompanied by bronchitis, as in measles, whooping-cough, and influenza. It also follows the inspiration of particles of septic matter, *aspiration pneumonia.* If there has been hypostatic congestion to predispose, *hypostatic pneumonia* may arise from the entrance of infectious particles.

In bronchopneumonia both lungs are generally diffusely involved, areas of consolidation being scattered throughout. On the pleural surface small nodular elevations, dark red or slightly reddish-gray in color, are seen. Are smooth on section. These areas are firm, and when separated from the surrounding tissue will sink in water. The lung in the immediate vicinity may be emphysematous, other portions being collapsed—atelectasis. Microscopically the alveoli are found to contain an exudate, albuminous in character, in which desquamated epithelial cells, leukocytes, and erythrocytes are

present. There is also a marked round-cell infiltration of the septa. The red blood-cells and the leukocytes are not, as a rule, found in large numbers unless the infection has been due to pyogenic organisms. The exudate may then be hemorrhagic or purulent; in either case gangrene may develop.

The lung returns to its normal condition through fatty degeneration of the exudate with absorption and expectoration.

Fibrous pneumonia is a chronic condition of the lung resulting from long-continued irritation and is characterized

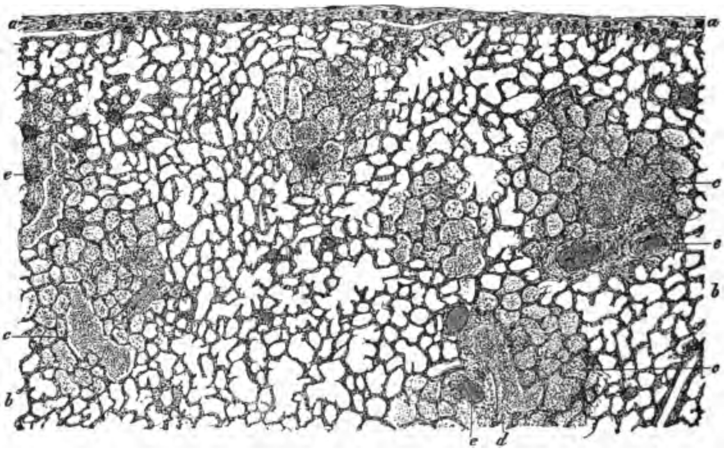

FIG. 126.—LOBULAR PNEUMONIA (ASPIRATION). × 8 (Ziegler). *a*, Pleura; *b*, lung; *c*, pneumonic areas; *d*, bronchiole; *e*, blood-vessels.

by an overgrowth of fibrous connective tissue. It may be divided into several forms according to its origin: (1) Pneumonokoniosis, those due to the inhalation of irritating particles; (2) those secondary to the acute pneumonias, chronic congestion or atelectasis; (3) pleurogenic, arising from chronic pleurisy; (4) those in which there is peribronchial and perivascular connective-tissue formation.

Pneumonokoniosis is a condition of the lung characterized by the presence of dust particles of various kinds. When

the fine particles gain entrance, they cause a catarrhal inflammation of the alveoli. Much of the dust may be expectorated, but some penetrates the interlobular connective tissue, where it may remain or be carried to the lymph-nodes. By acting purely as a mechanical irritant, or particularly if the particles are not aseptic, a productive inflammation

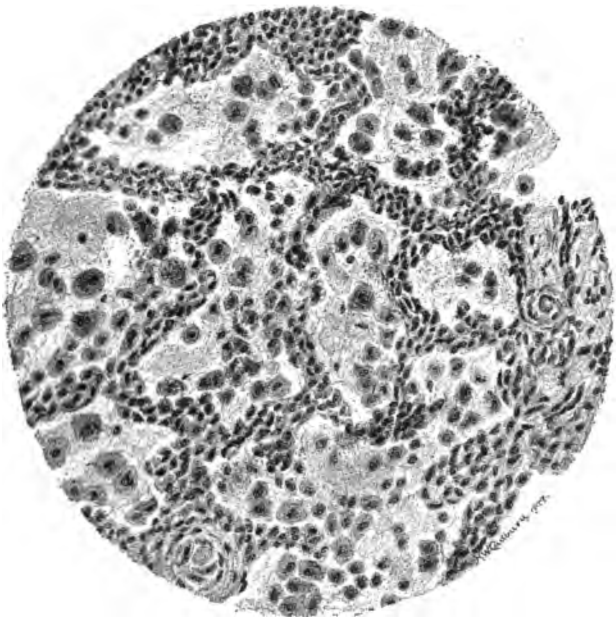

FIG. 127.—CATARRHAL PNEUMONIA, SHOWING DESQUAMATED EPITHELIAL CELLS IN THE ALEVOLAR SPACES (McFarland).

with the formation of fibrous tissue results. This occurs in both lung and lymphatic tissue.

Some of the foreign particles may get as far as the lymph-nodes in the fissure of the liver, and through involvement of a vein the dust can gain entrance into the circulation and be deposited in the liver and intestine.

From the irritation a lobular pneumonia may occur and

even cavities (non-tubercular) form. There is always found at post mortem some dust inhalation, the amount depending upon the environment of the individual.

According to the kind of particles inhaled, the condition receives various names: *Anthracosis*, when coal-dust; *siderosis*, metal dust; *chalicosis*, stone dust.

Secondary fibrous pneumonia results from an overgrowth of the connective tissue of the septa, which become much thickened. There is also proliferation involving the alveolar exudate.

The *pleurogenic* form of fibrous pneumonia results from chronic pleurisy. The lung shows numerous large and thickened trabeculæ of fibrous tissue extending from the surface deep into the interior of the organ.

The *peribronchial and perivascular* forms present an overgrowth of connective tissue in varying degrees, about the bronchi and vessels. A moderate form of this is found in all the varieties of fibrous pneumonia.

Purulent pneumonia is one caused by pyogenic organisms. In it there is found a purulent and hemorrhagic exudation, both in the alveoli and fibrous septa. The infection may take place through the bronchi, *bronchogenic;* the blood, *hematogenic;* or through the lymphatics of the pleura, *pleurogenic*.

The *bronchogenic* variety is most marked in the aspiration pneumonias that follow suppurative lesions of the upper air-passages. Large and small purulent collections are found, both in the alveolar walls and within the alveoli as well.

The *hematogenic* form is secondary to purulent areas in other parts of the body. The infectious agents gain entrance into the circulation, and as emboli are carried to the capillaries of the lung. Becoming lodged they set up secondary suppurative changes. Hemorrhagic infarctions are frequently found. The central part is necrotic, while around it is found a zone of severe infiltration. The entire area may soften, break down and form cavities. The abscesses quite frequently evacuate into a bronchus or sometimes into the pleural cavity, giving rise to *empyema*, a purulent pleurisy. Gangrene of the lung may occur.

Pleurogenic pneumonia is a form that has its origin in an inflammation of the pleura. Involvement takes place not only by contiguity but by extension into the deeper portions of the lung by way of the lymphatics—purulent lymphangitis. Abscesses of the lung may be caused in the same way by an extension of an empyema. The lobules of the lung may be separated by bands of suppurating tissue (dissecting pneumonia). There is thickening of the surface of the lung and of the pleura due to an extensive round-cell infiltration.

Gangrene.—This follows the entrance of saprophytic organisms into lung tissue that has undergone degenerative changes. The primary necrosis may follow in the course of pneumonia, tuberculosis, embolism, and infarction. May also result from the aspiration of putrefactive material, as in gangrene of the larynx, foreign bodies in the bronchi; extension of disease of neighboring tissues, as in carcinoma of the esophagus with perforation.

An *idiopathic* form occurs in alcoholics and in asthenic states.

The involvement may be either *diffuse* or *circumscribed.* In the latter, there are usually numerous irregular areas of a dark brown, greenish, or black color. They are rather dry, and are surrounded by a zone of congestion and edema.

In the diffuse variety the condition is much more severe. It may follow the circumscribed form or occur primarily. The gangrene is of the moist variety, the affected area being soft, mushy, greenish in color, and having an extremely foul odor.

The broken-down tissue may be expectorated and leave a cavity through which blood-vessels and bronchi may pass. Generally the vessels are obliterated by means of an arteritis with thrombus formation. The artery may, however, be destroyed before such a protective measure has taken place and severe hemorrhage result.

General embolism with septicemia frequently occurs. If recovery follows the disappeared necrotic tissue is replaced by connective-tissue hyperplasia.

The sputum in gangrene of the lungs is extremely offen-

sive and tends to separate into layers—an upper frothy one, a middle, yellowish and fluid, and a lower layer that is brownish and purulent. In the sediment are found particles of lung tissue, triple phosphate crystals, margaric acid, pus cells, pigment, and fat drops. Numerous organisms of various kinds are also present.

Infectious Diseases

Tuberculosis.—Is caused by the tubercle bacillus and may be either a local disease or a part of a general involvement. The infection may gain entrance to the lungs in three ways: by the air, *aërogenic* or *bronchogenic;* by the blood, *hematogenic;* or by the lymph-channels, *lymphogenic.* All three methods are finally closely associated.

Aërogenic Tuberculosis.—The tubercle bacilli gain entrance by adhering to dust particles. They pass down the bronchi, finally becoming lodged upon the mucous membrane of either the air-vesicles or the terminal bronchioles. The apex of the lung is the portion generally involved at first. The bacilli act upon the mucosa as an irritant and set up a mild catarrhal inflammation. The alveoli become filled with desquamated epithelium and leukocytes. This constitutes the primitive tubercle. The bacilli may grow in the air-cells or may be carried by the leukocytes into the lymphatics, so that the original tubercle may be either *alveolar* or *in-interstitial*, or, if around the bronchi, *peribronchial.* As the organisms increase in number there is an increase in the extent of the tubercle, thus involving neighboring alveoli. These undergo the same changes as the one originally infected. As this process extends there is destruction of the capillary vessels in the tubercles, and as no new ones are formed, there is a loss of nutrition. As a result there is coagulation necrosis of the central part of the tubercle. While this is taking place there is a proliferation of the fixed connective-tissue cells in the structures surrounding the diseased area; round-cell infiltration also occurs.

The tubercle, as it increases in size, approaches and coalesces with neighboring ones till large areas form. The central

portion, showing coagulation necrosis, finally opens into a bronchus, escapes, and leaves a ragged cavity behind. Blood-vessels will be exposed, and if destruction occurs before obstructive endarteritis takes place there will be hemorrhages of varying degrees of severity. The bronchus may be evident or its walls may have been completely destroyed.

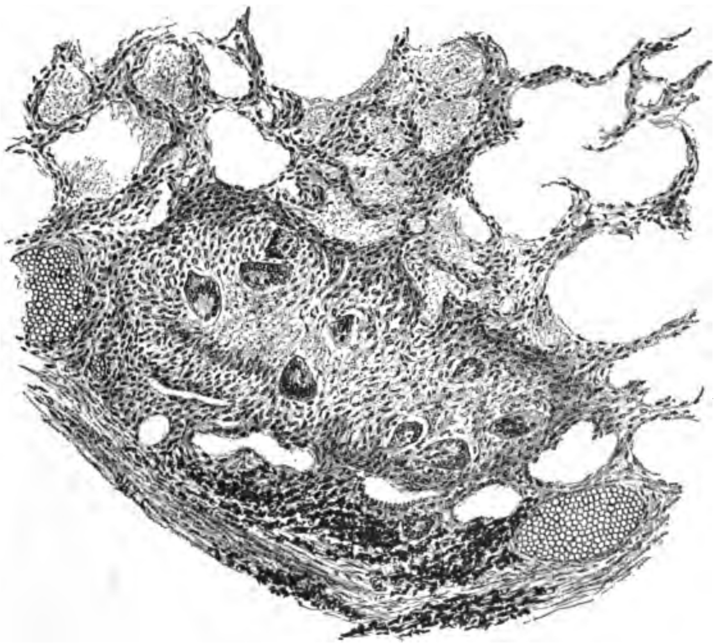

FIG. 128.—PERIBRONCHIAL TUBERCLE OF THE LUNG AND CASEOUS PNEUMONIA OF THE ADJACENT ALVEOLI (Stengel).

When communication has been effected between a tubercular focus and the outside air secondary infection by pyogenic organisms occurs. At the same time the tubercular material is carried along the bronchi during the respiratory acts and other foci are established. The lymphatics carry the bacilli into other parts and there is also involvement of the blood-

channels. Consequently all three methods of infection are being made use of and the entire lung may become converted into one mass of broken-down caseous material.

In the bronchogenic form the caseation is particularly marked, while in the hematogenic and lymphogenic the involvement is more distinctly miliary. Of the caseous, three

FIG. 129.—SUBACUTE CASEOUS (TUBERCULOUS) PNEUMONIA (Bollinger).

different forms are described: The *acute caseous* or *galloping* phthisis; the *chronic ulcerative*, and the *fibrous* or *fibroid* type. This is not an accurate clinical division, as all three processes may be present in the same lung.

Acute caseous tuberculosis occurs most frequently in children. The process is usually quite rapid in this form and

the lung resembles somewhat closely the stage of gray hepatization of croupous pneumonia. The infection is at first lobular, but by extension may involve an entire lobe. Either the base or the apex is the seat of the primary focus. The cut surface of the lung will show irregular yellowish caseous areas with congestion of the intervening pulmonary tissue. The yellowish areas when closely examined will be seen to consist of bronchi surrounded by caseous material and more or less filled with the cheesy exudate. The lumen, as a rule, is very rarely obliterated completely. Numerous small excavations form, but there is little attempt at fibrous formation.

If the infection is less severe, there is less confluence of the degenerated areas, and instead of a general infiltration, scattered patches of caseous pneumonia are seen throughout the lung. There is also more fibrous growth, some of the areas becoming completely encapsulated.

Chronic ulcerative tuberculosis is the form most generally met with. It usually begins in the apices and is characterized by the formation of quite extensive cavities. These result from degeneration and necrosis of the lung tissue. Several cavities may coalesce and form a single large one. A large part of the ulcerative process is due to secondary infection by pyogenic organisms. The inner surface of the cavities is rough and irregular, arteries and strands of lung tissue being present. There is fibrous proliferation in the walls, while in the cavity itself there is a secretion containing broken-down caseous material, pus cells, epithelium, and tubercle bacilli and the organisms of the secondary infection.

The arteries traversing the cavities may be the seat of small aneurysms which may rupture and give rise to a fatal hemorrhage.

The healing processes, although well marked in places, are unable, as a rule, to keep pace with the necrosis, and the patient eventually succumbs.

Fibroid Tuberculosis.—This may occur as an essentially chronic condition or it may follow upon acute processes with cavity formation. Surrounding the caseous areas there is a proliferation of connective tissue with encapsulation and the

contained material may become completely infiltrated with lime salts. It may be merely surrounded by a capsule, and

FIG. 130.—TUBERCULOSIS OF THE LUNG (McFarland).
The upper lobe shows advanced cheesy consolidation with cavity-formation, bronchiectasis, and fibroid changes; the lower lobe retains its spongy texture, but contains numerous miliary tubercles.

if anything should occur that should cause destruction of the enveloping tissue, the caseous material could give rise to

acute processes, the activity of the tubercle bacillus not having suffered by its confinement.

The newly formed fibrous tissue is, in a way, of distinct disadvantage, as by its shrinking it causes distortion with diminishment in the size of the lung.

Hematogenous Pulmonary Tuberculosis.—This form results from the entrance of the infecting material into the blood-stream, and is usually part of a general tuberculosis of the body, but it may be limited to a single lung. The bacilli lodge in the capillaries in the form of emboli and set up minute foci of degeneration—*miliary tubercles.* These are small grayish areas formed in the same way as tubercles elsewhere. When the lungs are alone involved the condition is called *miliary tuberculosis of the lungs.*

Lymphogenic Tuberculosis.—In this the infection generally results from the bacilli being carried from the lymph-nodes, where they have lodged, into the lung tissue by means of the lymphatics. A tuberculous lymph-node may soften and discharge into a bronchus, a form of secondary aërogenous infection. Extension may occur from a tubercular pleurisy. In such cases there is frequently associated a suppurative lymphangitis. The processes in the lymphogenic form are quite similar to the hematogenic variety and show tubercle formation.

A patient recovers from tuberculosis when the lung becomes sufficiently immunized to resist further progress of the bacilli. In such cases the tubercles will have been encapsulated by new-formed fibrous tissue, isolated and calcified.

Tuberculosis of the lungs may be complicated by secondary infections elsewhere, particularly of the intestines. This results from the swallowing of the infectious sputum and is most common in adults. The larynx may be involved in the same way. There may be infection of the pleura with the formation of adhesions that can interfere very much with respiration. Lobar pneumonia may involve the non-tubercular areas of the lung or emphysema may be present. *Pneumothorax* may be caused by the tubercular process

rupturing into the pleural cavity, with collapse of the lung. There is usually an accompanying empyema resulting from the infection of the pleura by the discharged material. *Hemorrhage, hemoptysis*, is the most dangerous and common complication. It may follow the rupture of a small aneurysm or the erosion of a vessel before a thrombus has had time to form. It may be slight or very severe. Some of the blood may remain within the lung and, forming a good medium for the growth of saprophytic organisms, give rise to gangrene.

The apices are the most common primary seat. This is probably due to the fact that their bronchi come off at such an angle that they are easily obstructed; that on account of being furthest away from the entrance of the blood-vessels they are more poorly nourished, and that the apex undergoes the least distention during respiration.

Syphilis.—This may be either *congenital*, the lungs being involved as well as other parts of the body, or it may be *acquired.*

The congenital is the more common and occurs as *white pneumonia*, a diffuse form resembling bronchopneumonia. The lungs are whitish in color, completely airless, and firm. Microscopically there is a desquamation of the alveolar epithelium, an infiltration of leukoyctes, and a connective-tissue proliferation in the interalveolar and interlobular tissues. There is usually some proliferation of the adventitia of the blood-vessels, also of the intima, so that some of the vessels may be completely obliterated.

Gummata may be present in the new-born either alone or associated with diffuse lesions; are sometimes found in adults. They generally occur near the root of the lung, beneath the pleura, and are commonly few in number and more or less circumscribed. They frequently undergo caseation, and it may be very difficult, if not impossible, to distinguish them from tuberculosis, except by staining for the tubercle bacillus. These areas present the ordinary microscopic appearances of gummata. The blood-vessels, besides showing a thickening and a hyaline degeneration, are surrounded by a round-

cell infiltration. The caseous material may be expectorated and the cavity be obliterated by the formation of a cicatrix.

Glanders.—This is very rarely found in the lung in man. The Bacillus mallei may gain entrance by inhalation or by the blood, following infection of the skin. In the first form numerous grayish or yellow nodules, varying in size up to that of a pea, are found scattered throughout the lobes. They are made up of a mass of round cells and frequently undergo caseous degeneration.

When infection takes place by the blood there is a diffuse purulent infiltration of large areas of lung, with the formation of abscesses and associated hemorrhagic infiltration.

Actinomycosis.—Seldom occurs. It may result from aspiration of the infecting organism, but is more often a secondary condition following actinomycosis of the upper air-passages or of the anterior or posterior mediastinum. There may be a single focus of infection in the form of a cavity containing a thick cheesy and purulent material in which the characteristic yellowish actinomyces granules are present. The lesions may be more general and nodular, these nodes tending to undergo central softening. On account of proliferation of the surrounding connective tissue they may closely resemble tubercles.

Tumors.—Primary growths in the lungs are unusual; secondary ones somewhat more common. Of the connective-tissue variety, small *fibromata*, *lipomata*, *chondromata*, and *osteomata* are found. *Primary sarcoma* is more common than the above and probably originates within the peribronchial lymph-nodes as a small round-cell or spindle-cell tumor. May have primary *endotheliomata* of the pleura with extension into the lung.

Secondary sarcoma of the lung is very common. It occurs in nearly every case of primary sarcoma elsewhere. Numerous small scattered nodules are found. These are whitish in color and frequently undergo softening.

Primary carcinoma is very rare, but it may develop from the mucous glands of the bronchi or a squamous epithelioma from the epithelium of the terminal bronchi and alveoli.

Secondary carcinoma is not as common as secondary sarcoma. It results from emboli of tumor cells lodging in the capillaries. May follow extension of an esophageal or mammary carcinoma. Sometimes may have secondary growths resulting from the inspiration of cellular particles of a carcinoma of the mouth or upper air-passages. Such cases may be associated with areas of bronchopneumonia.

Adenomata have been met with and *dermoid cysts* occasionally appear.

In *leukemia* numerous miliary growths consisting of small round cells may be found. They resemble tubercles except that they are somewhat whiter and softer, but do not tend to undergo caseous changes.

Parasites.—Besides the specific organisms mentioned various vegetable parasites, as the *aspergillus*, the *mucor*, and the *oïdium*, may be met. Are found at times in tubercular cavities. May give rise to a *pneumonomycosis aspergillana.*

Animal parasites such as the *lung fluke* are sometimes found. It gains lodgment near the root of the bronchi and discharges its eggs into the mucopurulent secretion that it excites. The eggs are found in the sputum. May give rise to hemoptysis. The *cysticercus cellulosæ*, the *strongylus longivaginatus*, *monas*, *cercomonas*, *coccidia*, and *psorosperms*, may all be occasionally found in the lung.

The most important is the *echinococcus*. It is usually secondary to primary disease of the liver and is most common in the lower right lobe. There are one or more cysts which may vary greatly in size. As a rule, the cyst occasions no symptoms, becoming inspissated and calcified. Sometimes it ruptures into a bronchus; in such a case the cystic contents will be expectorated and in the sputum characteristic booklets can be found. An empyema can be caused by the cyst rupturing into the pleural cavity.

DISEASES OF THE PLEURA

Secondary involvements are more common than primary diseases on account of the relation of the pleura to the lung.

Active hyperemia is an early stage of pleuritis.

Passive hyperemia occurs in diseases in which there is interference with respiration; is most common as a result of venous stasis due to cardiac disturbances. *Hydrothorax* may result from it.

Hemorrhage. If there is extreme congestion petechiæ will be found. Are most marked in death from suffocation, but also occur in diseases of the blood and in hemorrhagic diatheses.

Large hemorrhages may result from traumatism, from rupture of large aneurysms, from fractured ribs, and from malignant tumors.

The blood that escapes into the pleura will not coagulate, as a rule, and is slowly absorbed if it has not become infected. Adhesions will form to some extent.

Hydrothorax is a condition in which both pleural cavities as a rule contain a watery, straw-colored fluid of a low specific gravity that does not undergo spontaneous coagulation. It occurs in chronic heart and kidney disease as a part of a general dropsy. The pleura is frequently opaque and lustreless and edematous. The lymph-channels are dilated and the endothelial cells may desquamate. From the pressure of the fluid the lungs are pushed backward and may be so much compressed as to interfere greatly with respiration. The lung may be even atelectatic. The effusion may occur suddenly, as in carbon monoxid poisoning, or be very chronic.

Is generally a slight effusion into the pleural cavities just before death.

Pneumothorax is the entrance of air into the pleural sacs. Is the result of accident and is almost invariably followed by infection and empyema. It results generally from the rupture of a tuberculous lesion, from gangrene or abscess of the lung, or from the rupture of an emphysematous air-vesicle. May be due to perforating wounds of the chest, to the rupture of an empyema into the lung, or from perforation of a gastric ulcer.

With each inspiration air escapes from the lung into the pleural sac until the pressure becomes so great as to seriously interfere with the expansion of the organ. The lung is pushed

backward and is much compressed. The opposite organ is displaced to one side, the diaphragm downward, and the intercostal spaces bulge.

The air may be absorbed, but as a rule infection occurs, giving rise to a *pyopneumothorax*, a combination of air and a purulent exudate.

Pleurisy or pleuritis is an inflammation of the pleura. It may be either primary or secondary. Most commonly occurs in the course of inflammations of the lung, as in pneumonia, tuberculosis, and gangrene. Also from involvement in inflammatory conditions of the pericardium, of the spine, the ribs or the chest wall. May be the part of a general infectious process, as acute articular rheumatism, or septicemia.

Many micro-organisms have been found, as the streptococci and staphylococci, colon bacillus, tubercle bacillus, pneumococcus and many others.

The involvement may be *local* or *general* and, according to the variety of exudate, *fibrinous*, *serofibrinous*, *purulent*, and *hemorrhagic*.

A single case of pleurisy may pass through all the above stages. In them all the pleura becomes hyperemic, and instead of being smooth and glistening, is rough and dull; the two layers of pleura do not glide with ease and an exudate escapes into the cavity.

In *fibrinous pleurisy* there is soon an exudate of fibrin forming a thin yellowish layer on the surface. It may increase in thickness and cause the pleural surfaces to adhere slightly, giving rise to the so-called "bread and butter" pleurisy. This exudate is composed of flakes and masses of fibrin containing leukocytes. The endothelium below is thickened and in places has desquamated. The sub-endothelial connective tissue is infiltrated by round cells and the vessels are congested.

The exudate may be absorbed completely, but if there has been much fibrin formation adhesions of varying density result. New capillaries penetrate the fibrin masses, the fibroblastic cells proliferate, and organization takes place. These bands, although at first delicate, soon become very dense.

They may be so extensive as to cause almost complete

obliteration of the pleural cavity, or be present in scattered areas only. There may be areas on the surface of the pleura of marked chronic thickening.

Serofibrinous Pleuritis.—In this variety there is a large amount of serous exudate as well as fibrinous. It may follow the fibrinous form, but usually begins with a serous outpouring. The fluid is denser than that in hydrothorax, and contains bits of fibrin as well as red and white blood-cells in small numbers. The amount of fluid may be very little or as high as several liters. The exudate may become somewhat hemorrhagic if large numbers of erythrocytes are present. The lung is pushed backward and the neighboring organs pressed upon.

Hemorrhagic pleuritis is generally the result of tuberculosis or of malignant disease of the pleura. The exudate is chiefly serous, with red blood-cells present, but at times may be almost pure blood.

Empyema or purulent pleuritis is the result of infection by some one of many micro-organisms. It may begin as a purulent pleurisy or it may follow infection of a sero-fibrinous pleuritis. It may result from some traumatism causing an opening into the pleural sac or occur in the course of disease of the lung. In the adult its cause is most frequently the streptococcus, in children the pneumococcus. Tubercular infection in adults is nearly twice as frequent as in children. The infecting organism, whatever it is, can be carried to the pleura either by means of the lymphatics or the blood-vessels. The organisms most commonly found are the streptococcus, pneumococcus, tubercle bacillus, staphylococcus.

In the pleural cavity there is found a small or a large amount of a cloudy purulent fluid which contains great numbers of pus-cells. The color may be at times greenish, although usually yellowish. The pleuræ are generally thickened and congested and covered with flakes of fibrin and degenerated endothelium. The pus may be completely absorbed and the two inflamed pleuræ unite with dense adhesions, or it may become cheesy and undergo calcareous infiltration. The changes are most marked in the visceral

pleura, which becomes greatly thickened and at first is soft and edematous, while fluid is still present. When the exudate disappears it becomes very hard and callous.

During the course of the empyema there is always more or less involvement of the lung. The fluid by its presence tends to push the lung backward and compress it. This may continue till expansion is impossible and atelectasis occurs. There may be an infection with resulting pleurogenic pneumonia. Rupture of the empyema into the lung sometimes happens, in which case the result is generally fatal.

Tuberculosis of the pleura is rare as a primary lesion; is usually secondary to similar disease of the lung or adjacent tissues. The primary form occurs as small, round, pearly bodies about the size of a pea. The pleura may be involved in the course of a general hematogenic infection. Will vary greatly in appearance; many small miliary tubercles in some cases, while in others the pleura may be covered by a widespread exudate. The fluid present may be sero-fibrinous, purulent, or hemorrhagic. It may become inspissated and calcification take place.

Syphilis of the pleura may be present as a part of a general syphilitic infection, but it is unimportant clinically and difficult to recognize at any time.

Tumors of the pleura are not very common, the most frequent variety being the *endothelioma*. It may be present as a diffuse infiltration of the pleura, resembling somewhat old adhesions, or in nodules scattered about. Secondary growths, as *sarcoma* or *carcinoma*, may result by metastasis or by direct extension from malignant disease of adjacent tissue, particularly by extension of carcinoma of the mammary gland through the chest wall. Other varieties found are the fibroma, lipoma, osteoma, and chondroma.

Parasites.—Echinococcus cysts are occasionally found.

CHAPTER XXI

DISEASES OF THE DIGESTIVE SYSTEM

Malformations.—The most common deformities are *cleft palate* and *hare-lip.* The former results from a failure of closure of the hard palate and is usually to one side of the mid-line. Hare-lip is the result of failure of union between the superior and premaxillary bones. May be single or double. The tongue may be either unusually large or small. Lack of development of the symphyses of the lower jaw sometimes occurs.

The *lips* may be the seat of ulcers and fissures and sometimes of a chronic inflammation with thickening.

Anemia of the mucous membranes of the mouth and lips is commonly seen in cases of general anemia and is a well recognized symptom.

Active hyperemia is found in inflammations and as an early symptom in certain infectious diseases. Passive hyperemia occurs in the general congestion of chronic lung and heart disease. Actual bleeding is found in scurvy and purpura and sometimes in the infectious fevers.

Stomatitis.—Inflammation of the mouth results from many causes, but particularly from local infection by bacteria. It differs greatly in severity and is divided into catarrhal, ulcerative, mycotic, and gangrenous forms.

Catarrhal Stomatitis.—This, the commonest form, results from the action of irritants, such as hot liquids, chemicals, decaying teeth, or from a depressed condition of the general system. There is marked hyperemia with desquamation of the epithelium. In chronic cases there is frequently a thickening of the mucous membrane with the formation of whitish areas. The mucous glands may enlarge and form small

cysts. Associated with the stomatitis there is an increased activity of the salivary glands.

Ulcerative stomatitis is usually found in children who are not well nourished. Occurs in malnutrition, tuberculosis, and in other chronic conditions, also in mineral poisonings, particularly by mercury and phosphorus. Is met with most commonly on the gums, although other parts may be involved. The gums become red and swollen and even hemorrhagic at the junction with the teeth. They become changed into a soft, necrotic mass that bleeds readily. The epithelium is destroyed and deep ulcers form; suppuration may ensue and the teeth become so loosened that they fall out. The inflammatory process may extend to the cheek and the tongue. There is marked increase of saliva, which has a bad odor. Mercury in small doses may cause it in some people who are especially susceptible; is then known as salivation.

Mycotic stomatitis is that which is directly due to micro-organismal infection. Of this variety *aphthous* or *follicular stomatitis* is an example. It occurs usually in children who are in poor physical condition. On the mucous membranes of the mouth there appear small whitish spots surrounded by an inflammatory zone. These areas consist of degenerated epithelium and fibrin, and the condition is therefore sometimes spoken of as croupous stomatitis. Ulceration seldom occurs. The condition may last for some time, the exudate finally being absorbed and the epithelium regenerating.

Thrush is that variety of mycotic stomatitis caused by the *oïdium albicans* which involves those structures covered by squamous epithelium. The tongue is most frequently involved primarily, but secondary infections through contact may develop. Usually occurs in marasmatic infants, but sometimes in debilitated adults. There is at first a diffuse reddening of the mucous membrane, then the formation of patches of a shining, whitish false membrane that adhere at first rather tightly to the underlying tissue, but finally become loose. The patches may coalesce, forming large areas of a pseudo-membrane that is composed of desquamated epithelium and parasitic threads. If the membrane is re-

moved it soon reappears. The disease may spread from the tongue to the pharynx and esophagus, and it has been known to extend into the stomach and bronchi.

The oïdium albicans is a budding fungus resembling the yeast and forms long myceliæ. Can be cultivated upon acid media that contain sugar. Longer threads form when grown on an alkaline medium.

Gangrenous stomatitis or *noma* is a rapid necrotic process involving the mucous membrane of the cheek. It occurs in children whose general condition is extremely poor, either as the result of chronic or severe acute disease. At the angle of the lip on the buccal surface there appears a livid area that rapidly becomes gangrenous. Penetration through to the skin may occur or the process may remain localized in the mucous membrane. When the skin is involved there are vesicles formed and the tissue soon breaks down into a foul-smelling mass. Death from exhaustion and secondary infection usually follows. The slough may separate and the patient recover, with usually marked deformity from the cicatrization. Although more common in female children, noma may occur in either sex and at any age. This process has been met with in the genital regions.

Syphilitic stomatitis may occur either as the primary chancre or, what is more common, as the secondary mucous patch. The primary form may appear on the lip, tongue, or tonsil in either a soft or an indurated form. Is accompanied by enlargement of the lymph-nodes. The mucous patches are superficial ulcers following cellular infiltration. Other secondary lesions may be present. *Gumma* are also found either in the corners of the mouth or on the palate. Are generally small and prone to undergo softening with ulceration and subsequent cicatrization.

Tuberculosis may rarely be primary, but is usually secondary to infection from tuberculosis of the larynx or pharynx or by infected sputum. Usually involves the posterior portion of the tongue, where small nodular tubercles of a yellowish-red color appear. They soon degenerate and form ulcers with thickened edges. The lesions may very closely resemble epithelioma.

Actinomycosis may result from the infection of an abraded surface by the fungus. It generally gains entrance to the alveolar border of the jaw by way of carious teeth. The process is generally a slow one of swelling with destruction of the adjoining tissues. There may be quite widespread involvement of the lymphatic nodes of the neck and jaw.

Glossitis or inflammation of the tongue occurs either in a superficial or a deep form. In the *superficial* variety there is a desquamation of the epithelium. It may follow marked intestinal disorders or be the result of local irritations. The surface of the tongue becomes white or brown, due to the degenerated epithelium, particles of food, and bacteria. May become dry, hard, and fissured. If the superficial glossitis becomes chronic, local thickenings of the mucous membrane are formed. They are irregular, slightly elevated, whitish patches, which may spread and coalesce. Occasionally the thickened epithelium may desquamate and leave an ulcer. This variety is known as *leukoplakia* or *psoriasis linguæ.* Quite frequently secondary epitheliomata develop at the site of the lesion.

The *deeper* inflammations of the tongue generally result from injury and infection. The organ may become swollen, painful, and infiltrated by leukocytes; small abscesses may also form. Is usually some degeneration and atrophy of the muscles.

One form of inflammation of the tongue is known as *melanoglossia*, black tongue. The epithelium upon the papillæ, particularly the filiform variety, becomes greatly increased and gives rise to a hairy appearance. The color may be due to an increase of pigment in the epithelium or to a fungus mixed with which are particles of food and bacteria.

Tumors of all kinds are found within the mouth. Of the connective-tissue forms, *lipoma*, *fibroma*, *myxoma*, and *sarcoma* occur, also *lymphangioma* and *hemangioma*. *Adenoma* and *carcinoma* of the squamous type are found. *Sarcoma* generally appears upon the gums near the roots of the teeth and is known as *epulis;* is generally of the giant cell variety. Some epuli may be pure fibromata. The carcinoma is gener-

ally present in the form of the *squamous epithelioma*. Is found most commonly on the tongue at one side, where its course is quite rapid. It appears as a circumscribed hard swelling which soon breaks down and rapidly ulcerates. It soon involves the neighboring cheek and larynx, and gives metastases to the cervical and submaxillary lymph-nodes, and if excised it soon returns.

Cysts result from obstruction to the ducts of the mucous or salivary glands. A *ranula* is a cystic dilatation of Nuhn's glands situated under the tip of the tongue, which may be displaced backward and upward. A thick viscid fluid fills the cavity. *Dermoid* cysts are also found.

Macroglossia, thickening of the tongue, and *macrocheilia*, thickening of the lips, result from a lymphangioma. The lymphatic spaces are much distended and contain liquid and round cells. This condition is generally congenital; is met with in cretins.

THE TEETH

Malformations.—They may be unusually large or small, increased or decreased in number, or even entirely absent. In congenital syphilis the upper central incisors of the permanent set are frequently malformed, being deeply notched at the edge.

Inflammation may involve the surrounding alveolar periosteum or the pulp of the tooth. It may go on to pus formation with loosening and death of the teeth. *Caries* is generally the result of malnutrition or lack of care of the teeth. The enamel of the tooth is destroyed by lactic acid, which is formed by many varieties of bacteria. The organisms are then able to enter the canals in the dentin with subsequent disintegration. The tumors of the teeth have been described in Part I.

THE TONSILS AND PHARYNX

Anemia and hyperemia occur here just as elsewhere. Active hyperemia as a beginning of inflammation; passive, in chronic heart and lung disease, in which cases the veins may

be distinctly varicose. Edema is found in connection with inflammation and ulceration and may be quite marked. Hemorrhage may occur in purpura and in severe infectious fevers, as well as being the result of direct injury. The blood may form quite a tumor between the layers of the soft palate.

Tonsillitis, or inflammation of the tonsil, may be either acute or chronic. *Acute tonsillitis* may be either symptomatic of various diseases or it may be a true local primary condition as a consequence of direct infection. It is known as *catarrhal*, *lacunar* or *follicular*, and *phlegmonous*. In the catarrhal the tonsils are somewhat reddened, usually as a part of a catarrhal pharyngitis. The lacunar or follicular form is characterized by the presence of many small yellowish-white spots over the surface of the tonsil. Each spot represents a follicle that has become filled with an exudate made up of degenerated epithelium, and bacteria, as staphylococci, streptococci, pneumococci, and tubercle bacilli. The exudate from the lacunæ may extend over the surface of the tonsil, forming a covering that resembles diphtheritic pseudomembrane. The exudate within the lacunæ may become inspissated and calcify. If the infection passes through the bottom of the crypts into the deeper tissues phlegmonous tonsillitis may result. In this there is abscess formation as well as round-cell infiltration. These collections of pus may discharge into the mouth, open into the larynx or even involve the large vessels of the neck, perforation of the internal carotid having occurred.

In *chronic hypertrophic tonsillitis* there is an increase in size of the tonsils, due not only to a hyperplasia of the connective-tissue septa and reticulum, but also to a hyperplasia of the lymphoid follicles. The tonsils may become so hypertrophic as to almost meet in the middle line, and by so doing cause obstruction to breathing and swallowing.

This form is frequently accompanied by marked disturbance of the general health and development. Is often found in children, and as a result they breathe with their mouths open; their digestion is often impaired and their mentality may be distinctly lessened.

Instead of the above hypertrophic form, the involvement may be confined to the lacunæ, which are wider and deeper than normal. They become filled with an exudate that through decomposition can give rise to inflammatory processes in adjacent tissues.

Tonsillitis leptothricia is caused by infection of the tonsils by the Leptothrix buccalis. It usually occurs in the poorly nourished, but may occur in a strong, well-nourished individual. Over the surface of the tonsil are numerous spots covered by a thick, dense, dry, whitish exudate that is composed of masses of threads of the leptothrix. It is firmly adherent to the crypts and is removed with difficulty. It usually involves other portions of the pharynx, but does not occasion much inflammation of the surrounding tissues. It tends to run a chronic course not yielding readily to treatment.

Tuberculosis of the tonsils is quite common. Is generally primary and involves the cervical lymph-nodes secondarily. From there it may by extension gain access to the lungs and occasion tuberculosis within them. It may also give rise to a secondary involvement of the intestines.

Syphilis of the tonsils may occur as a primary, secondary, or tertiary lesion.

PHARYNX

Circulatory disturbances are usually a part of similar troubles of neighboring tissues.

Inflammation.—The *acute catarrhal pharyngitis* or *angina* may result from exposure to cold, to the irritating action of various substances, as tobacco smoke and dust, or may occur as a part of an intestinal derangement. The mucous membranes become red and swollen with decreased secretion at first. As the process goes on there is frequently an abundance of a thick, tenacious secretion composed of mucus and desquamated columnar epithelial cells. In severe cases true ulcers may form along the posterior wall.

In *chronic pharyngitis*, such as occurs in excessive smokers and in those who use their voice a great deal, the posterior

wall and the faucial pillars are particularly involved. There is chronic congestion and the lymphoid collections become hyperplastic, causing slight granular elevations. The secretions become less, as a rule, but may be increased and mucopurulent. The pharyngeal tonsils are usually hyperplastic.

Phlegmonous pharyngitis and *retropharyngeal abscess* follow the entrance of bacteria, usually pyogenic, into the deeper tissues or may result from caries of the spinal column. If there is rapid abscess formation there is bulging into the pharynx and rupture may take place. If the process has been slower the pus will extend along the deep fascia till perforation into the posterior mediastinum, bronchi, or esophagus occurs. General septicemia not infrequently occurs.

Syphilitic pharyngitis is common as a secondary symptom, but it has no characteristic appearance that renders it easily recognizable.

Tubercular pharyngitis is unusual.

Pseudomembranous pharyngitis may be diphtheritic or non-diphtheritic.

The *non-diphtheritic pharyngitis* is generally caused by the streptococcus pyogenes or may result from the action of very irritating substances, as steam or ammonia. The appearance of the pseudo-membrane is, to the naked eye, similar to that of the diphtheritic variety. It is not, however, accompanied by the same constitutional depression, nor is it followed by paralyses.

Diphtheritic pharyngitis is caused by the Klebs-Loeffler bacillus and characterized by a pseudo-membrane that is yellowish or dirty gray in color. The involvement may be limited to a small portion of the pharynx, being most common on the arches of the fauces, or the tonsils and nares as well may be concerned. It may extend even into the esophagus and stomach. This pseudo-membrane is laminated, being composed of fibrin in the meshes of which are desquamated epithelial cells, leukocytes and erythrocytes, and the diphtheria bacilli in great numbers. It is formed by the coagulation of the exudate and by coagulation necrosis of the superficial tissues.

This membrane can be removed, exposing a raw ulcerated surface upon which a new membrane quickly forms. The lymph-nodes near-by may enlarge and undergo suppuration.

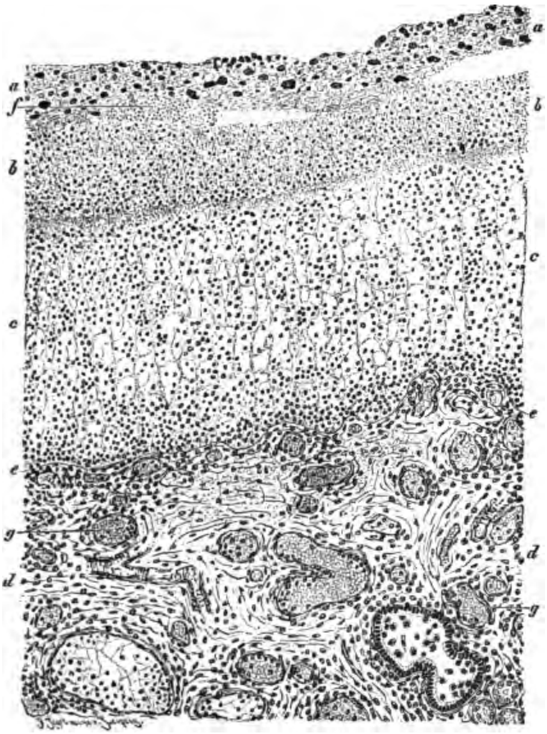

FIG. 131.—DIPHTHERIC MEMBRANE FROM THE UVULA. × 50 (Ziegler).

a, *b*, *c*, Layers of fibrin containing epithelial cells, leukocytes, and bacteria; *d*, *e*, cellular infiltration of the connective tissue; *f*, collections of red corpuscles; *g*, dilated blood-vessels.

The extent of the pseudo-membrane does not denote the gravity of the infection. The severity depends upon the virulence of the particular bacillus that has caused the infection; it is the expression of the intensity of the toxin present. In

severe forms it spreads rapidly, and if there is a mixed infection with streptococci, hemorrhage and gangrene may result, as well as secondary abscess formation elsewhere in the body. Besides the local manifestations there are marked general symptoms due to the presence of a dangerous toxin. The action of this body is seen in the form of small foci of necrosis in various tissues of the body. Death may result from cardiac paralysis resulting from the presence of the toxin.

Of the internal organs the liver especially shows focal necrosis, in which the cells are degenerated and the nuclei show hyperchromatosis. There is hyperemia of the kidney with cloudy swelling of the epithelium, edema, and hemorrhage. Myocarditis and degeneration of the cardiac muscle also occur. The spleen is also hyperemic.

During convalescence paralysis, particularly of the throat, may occur, also of the muscles of the eyes, the larynx, and the diaphragm. The muscles will show a round-cell infiltration between the fibers and a granular and fatty change of the cells.

There may be degeneration of the ganglion cells of the cord.

Tumors of the pharynx are rare. Squamous epithelioma as a result of extension is the most common, but fibromata and sarcomata have been encountered.

SALIVARY GLANDS

Inflammation of the parotid gland, *parotitis*, or *mumps*, occurs as an independent disease, possibly due to a small diplococcus described by Laveran. The infection probably occurs by way of the parotid duct; the gland becomes much swollen and tense on account of a marked serous exudation. Although abscess formation appears imminent, it is very unusual for suppuration to occur. The exudate can be absorbed and the gland return to a normal condition very rapidly. There may be a chronic induration remaining, or if abscess formation with rupture has taken place, a fistula may result. Secondary inflammation of the testicles or of the ovaries may occur either during the attack or shortly after the inflammation has subsided.

In the inflammation secondary to infectious diseases, as typhoid, scarlet fever, diphtheria, and others, suppuration is not so uncommon. Small abscesses may form and become confluent. The inflammation may become chronic with hyperplasia of the fibrous connective tissue, or it may subside and leave no traces.

Angina ludovici is a very severe form of inflammation of the submaxillary gland. The infection extends into the surrounding tissues, with suppuration and even gangrene. Abscesses form and discharge either externally or in the mouth; necrosis and gangrene are present and death frequently occurs. This disease may be the result of infection by means of carious teeth or infection of the gland itself during the course of an infectious disease, particularly scarlet fever.

Fistulæ of the salivary ducts may follow traumatism or the perforation of an abscess. The parotid duct is the one generally involved.

Concretions or calculi are sometimes found; are called *sialoliths*. They are composed of phosphate and carbonate of calcium, and are found in the smaller as well as the main duct. They frequently give rise to retention *cysts*, the most common variety being that known as *ranula*, a term applied not only to a cystic condition of Nuhn's glands but of the sublingual as well.

Tumors of the salivary glands are not uncommon, the parotid being most frequently involved, the connective-tissue tumors, as fibroma, lipoma, chondroma, and sarcoma, being the most usual. Adenoma and primary carcinoma are unusual. The most common neoplasm is the *mixed tumor* of the parotid. This is composed of sarcomatous tissue, along with cartilage, mucous and fibrous tissue. It grows slowly, does not frequently give metastasis, and when excised seldom returns. It is probably the result of fetal inclusions taking place during the closure of the first branchial cleft.

THE ESOPHAGUS

Malformations.—It may terminate in a blind pouch in its upper portion; it may be double or completely wanting.

Fistulæ opening into the pharynx and neck are the result of incomplete closure of the branchial arches.

Circulatory disturbances may be part of a general condition. In diseases of the heart, lungs, and in cirrhosis of the liver passive congestion with varicose veins may be present.

Inflammation of the esophagus, *esophagitis*, may be the result of irritation of foreign bodies, as hot liquids, acids, and alkalies, or of infection. In the *catarrhal* type there is hyperemia, infiltration of the mucous coat, and desquamation of epithelium, with occasional ulcer formation. If the process becomes *chronic*, as in long-continued passive congestion and in alcoholics, the mucous membrane is thickened, and thrown into folds; is dark in color, ulcers are present, and there may be hypertrophy of the muscular coat.

Pseudo-membranous esophagitis may be the result of infection by the streptococcus or by the diphtheria bacillus; is usually secondary to extension from neighboring tissues that were primarily involved.

Suppurative esophagitis may result from the extension of inflammation from the mucosa to the submucous coat, or it may be due to traumatism involving the deeper tissues.

In *smallpox* ulcers may form as a result of the eruption of pustules and *thrush* may extend from the mouth.

Stenosis of the esophagus may be the result of interference from within or from without. *Compression* by tumors, aneurysms, or other lesions. *Strictures* may be very marked. They usually result from the contraction of cicatrices formed in the healing of ulcers due to the swallowing of destructive liquids, as acids and alkalies. May be caused by syphilis, a rare occurrence. Carcinoma may cause stenosis by projecting into the lumen or by contracting the walls.

Dilatation of the esophagus is the result of an obstruction and usually occurs at the cardiac end, where it passes through the diaphragm into the stomach. Sometimes dilatation occurs without stenosis, in which case the esophagus is in the form of a pouch, largest at its center.

Diverticula or local sacculations of the esophageal wall

may be due to pressure from within, *pulsion diverticula*, or to traction from without, *traction diverticula*.

The *pulsion diverticula* are more common at the upper part of the tube, where the greatest pressure occurs. There is loss of tone of the muscular coat and the mucous membrane projects in the form of a pouch from the posterior wall at the pharyngeal junction. They may be very small or as large as a pear. They communicate with the lumen of the esophagus and become filled with food which is retained. This frequently undergoes decomposition and sets up inflammatory changes in the mucosa and adjacent tissues.

Traction diverticula are more common and are found near the lower end of the esophagus at the bifurcation of the trachea. They are the result of the contraction of adhesions of diseased bronchial glands. Are generally on the anterior wall and are conical in shape with the apex directed outward at the seat of the adhesion. There may be no change in the constituents of the wall, or the muscular coat may be lacking. Perforation may occur if the tension at the apex becomes too great. Escape of the contents may take place into the pleura, pericardium, or lungs. Death may result from hemorrhage following perforation of a pulmonary artery.

Perforation of the esophagus may depend upon causes acting either from within or from without. It may follow from ulcerations caused by the pressure of the cricoid cartilage in bed-ridden patients, or from syphilitic or cancerous ulcers. It may be due to outside pressure from caseating glands, abscesses, gummata, or aneurysms of the aorta. Rupture may be the result of traumatism or be spontaneous. Inflammation to the grade of gangrene may follow the escape of material from the perforated esophagus. If the gastric contents regurgitate there may be a partial digestion of the walls of the esophagus. This may, however, be a post-mortem condition.

Tumors are not very common, although of the connective-tissue tumors the fibroma, myxoma, myoma, lipoma, and more rarely sarcoma have been observed. The most common growth is the *squamous epithelioma*. It is most fre-

quently found in the lower third at the place where the left bronchus crosses over. The growth is flat, more or less ring-like, and usually ulcerated. The mucous coat is destroyed and papillary projections extend into the esophagus and cause obstruction of the lumen. The submucosa and the muscular coat may become infiltrated and the adjacent tissues also involved. There is stenosis with subsequent dilatation above the tumor. Food is retained and ulceration with perforation may occur. Metastatic growths are found in the neighboring lymph-nodes, bronchi, pleura, lungs, and liver.

THE STOMACH

Malformation.—It may be completely absent, or abnormally small, with atresia or stenosis of the pylorus, or it may be in the form of two pouches connected by a smaller tube (hour-glass stomach). The stomach may be reversed in its position in transposition of the viscera.

Circulatory Disturbances.—*Anemia* occurs in cases of general anemia, accompanied, if long continued, by fatty degeneration and atrophy of the mucous membrane. The mucosa is thin and frequently smooth. *Active hyperemia* is present normally during digestion, and is widespread. If the result of irritation, the color is more intense and is distributed in irregular streaks or patches, particularly on the tops of the rugæ. *Passive hyperemia* is the result of venous stasis in chronic heart and lung diseases and cirrhosis of the liver. The mucosa is purplish in color, swollen, and edematous. Small punctate hemorrhages may occur and also small erosions. The changes are most marked near the pyloric end.

Hemorrhage of varying severity frequently occurs. The punctate form, that is found so repeatedly at post-mortems, is in many cases the result of vomiting during the last moments of life. It may also result from congestion and inflammation, or be met with in various infectious and hemorrhagic diseases. If examined carefully, it can generally be seen that over these hemorrhagic points there is a loss of epithelium. The mucosa not being properly nourished at

that point is unable to withstand the action of the gastric juice.

Massive hemorrhage occurs in destruction of the mucosa in the course of gastric ulcer and gastric carcinoma. In the peptic ulcer the bleeding usually comes from the erosion of a single blood-vessel and may be so great as to cause death. In the carcinoma there is a slow oozing from degenerated capillaries, with the "coffee-grounds vomit," blood that has been acted upon by the gastric juices. *Melæna neonatorum*, vomiting of blood by new-born infants, is accompanied by the formation of ulcers of the gastric mucosa. It apparently results from imperfect respiration, causing a backing up of the blood. By many it is thought to be due to some cerebral lesion.

Thrombosis of the gastric vessels is rare, but is thought by many to be a cause of peptic ulcer and also of the ulcers that are found in the stomach and duodenum in cases of extensive burns. *Embolism* is more common; occurs in the course of cardiac disease.

Inflammation or Gastritis.—The *acute* form is generally due to the irritation of certain substances taken into the stomach and is commonly found at the pyloric end. The mucosa is red, thickened, and covered by mucous secretion, and punctate hemorrhages are occasionally present. Microscopically the epithelial cells are found to be the seat of cloudy swelling, numerous goblet cells are present, and there is an infiltration of round cells. The lymph follicles are also frequently hyperplastic.

Pseudo-membranous gastritis may be due to the action of caustic substances or to some of the infectious fevers, as smallpox and scarlatina. It may also be the result of the extension of a true diphtheritic process. The mucosa is covered by patches of a grayish-white pseudo-membrane under which the necrotic process may have involved the entire mucosa.

Phlegmonous gastritis is very rare, but sometimes follows the entrance of streptococci. The submucosa and muscularis become swollen and infiltrated by pus cells even to the

extent of more or less circumscribed abscesses. These may finally rupture into the cavity of the stomach. Healing takes place by the extension of the epithelium from the neighboring tissues into the opening resulting from the rupture of the abscess.

FIG. 132.—CHRONIC GASTRITIS (McFarland).

The mucosa is infiltrated with leukocytes, the glandular tissue has in part disappeared, and some of the glands (*a*) have developed into cysts; *b*, mucosa; *c*, submucosa.

Chronic gastritis may be the result of repeated acute attacks or it may have been chronic in form from the onset. It follows the abuse of alcohol, results from the eating of improper food, and occurs also in the course of various con-

stitutional diseases. Chronic congestion predisposes. In the *simple* chronic variety the mucosa is thickened, hyperplastic, and infiltrated, and bands of connective tissue surround projecting areas of epithelium. This is most marked at the pyloric end, where the mucosa may be markedly wrinkled and is associated with polypoid projections. *Sclerotic* or *interstitial* gastritis probably is due to the long-continued action of a mild irritant. There is an increase of the connective tissue, which as it contracts causes atrophy of the glands. The mucosa is very much thinner than normal, grayish in color, and in places there are frequently seen large but slight ulcerations. From the contraction of the new-formed connective tissue stenosis of the pylorus sometimes occurs.

Peptic or round ulcer is a peculiar form of ulceration generally found in the posterior wall in the lesser curvature at the pyloric end of the stomach, and probably due to the action of the gastric juice. It is thought to be due to a thrombosis in a vessel giving rise to a local area of necrosis, which being no longer able to resist the action of the gastric juices undergoes digestion. Infection, embolism, infarction, spasmodic contractions of the blood-vessels, are all thought to have some bearing upon the formation of these ulcers. They are found most frequently in chlorotic girls in whom there is an associated increase in the acidity of the gastric juice. The peptic ulcer is usually single and small, but is sometimes multiple and large. It is generally round or slightly oval, wider at the top than at the bottom, and is accompanied by very little inflammation. The mucous layer alone may be involved, or the destruction may extend to the submucosa, the muscularis, or even to the serous covering. In healing there is cicatricial tissue formed which on contracting gives rise to a peculiar white stellate scar. If the ulcer was in the region of the pylorus, stenosis of that outlet may result. From the floor of the healed ulcer carcinoma sometimes develops. The two dangerous results are perforation or hemorrhage. The perforation is usually smooth and round and looks as if it had been punched out. Sometimes there have been ad-

hesions to neighboring organs, so that damage is prevented, but more frequently the gastric contents will escape into the abdominal cavity and give rise to peritonitis. Hemorrhage is the result of ulceration of a large arterial branch. This is more common than perforation. The amount of blood lost may cause death or there may be merely a constant oozing.

Peptic ulcers sometimes occur in the upper end of the duodenum close to the pyloric orifice and also in the lower portion of the esophagus.

Atrophy of the glands results from chronic inflammation and is also found in old age and in cases of pernicious anemia.

Fatty metamorphosis of the glandular epithelium may follow phosphorous poisoning or occur in the course of severe infectious diseases. The mucous membrane is duller and more yellowish than usual.

Amyloid change is present chiefly in the muscularis, but also to a slight extent in the mucosa. It generally first appears in the walls of the smaller arteries of the submucosa.

Pigmentation of the mucosa is the result of numerous small hemorrhages or occurs as a part of a general discoloration often seen in chronic malaria. The mucosa is of a dark, slaty discoloration.

Calcification of the stomach in small areas has sometimes been found in certain poisonings, such as bichlorid of mercury, that are accompanied by rapid absorption of lime salts from the bones. Particles of calcium carbonate are found in the interstitial tissue.

Gastromalacia is a condition of softening of the stomach walls due to post-mortem changes resulting from the action of the gastric juices. Is most marked when there is hyperacidity and in that part of the stomach that has been most dependent. If the organ was anemic the mucous membrane appears pale gray in color and somewhat gelatinous in consistency. If congestion was present the mucosa will be dark brown. This is particularly marked along the veins, the hemoglobin being transformed into hematin. Sometimes perforation may occur, but this can be recognized readily, as there will be no local inflammatory reaction or peritonitis.

Gastroptosis is a downward displacement of the organ either acquired or congenital, and is very frequently a part of a general displacing or *splanchnoptosis* of all the abdominal viscera.

Dilatation or gastrectasis is usually due to some obstruction at the pyloric outlet. Food is retained; this undergoes fermentation and the stomach walls become weaker than ever. This may continue until the organ becomes enormously distended, the mucosa becoming very thin and atrophic. The stomach may be so greatly dilated that the greater curvature will extend not only below the umbilicus, but even down into the pelvis. There may be also a displacement in position, the organ lying almost perpendicularly. Dilatation may also be due to the contraction of adhesions to the outer surface of the stomach.

In some cases, the atonic form, there is a weakening and a relaxation of the walls without any obstruction at the pylorus. In gastrectasis there may be most marked indications of malnutrition.

Tuberculosis is extremely rare and **syphilitic** lesions but little more frequent, although gummata may be found. Sometimes a diffuse cirrhosis of all the gastric coats may be found in syphilitics.

Anthrax, actinomycosis, and **glanders** have been described.

Tumors.—The connective-tissue tumors, as *fibroma*, *myoma*, and *lipoma*, have been occasionally found. *Sarcoma* is more rare; it seems to originate within the lymphoid deposits and is generally round-cell in character. Polypoid projections of the mucous membrane are sometimes confused with tumors, but they are not neoplastic, are the result of chronic inflammations, and are sometimes cystic.

Adenomata have been found, but they are unusual, as they generally very quickly undergo a carcinomatous degeneration.

Carcinoma is not uncommon and is nearly always primary. It is more frequent in men than in women, usually in middle or advanced life. Its most frequent seat is at the pyloric end

of the stomach, on the posterior wall of the lesser curvature. It sometimes first appears at the cardiac end. The walls may be more or less involved in the process. The appearance of the growth differs greatly according to its histologic characteristics.

Scirrhus cancer is usually situated at the pyloric opening, which may be completely or partially surrounded. The walls are thickened and indurated. The opening is much stenosed and the mucous surface may be smooth or irregular

FIG. 133.—SCIRRHUS OF THE PYLORUS, CAUSING PYLORIC STENOSIS (Orth). *D*, Duodenum; *P*, pylorus; K, carcinomatous projections on the mucosa.

with depressed and ulcerated areas. Microscopically there will be seen large amounts of dense connective tissue with a few atypical epithelial cells.

Medullary carcinoma generally appears at the pylorus, but sometimes on the wall in the lesser curvature. The growth is irregularly elevated, spongy, and cauliflower-like. Is soft and vascular and ulcerated, particularly in the center, thus forming a crater-like excavation where perforation may occur. Microscopically the epithelium predominates and retains to some extent the normal arrangement, although the

individual cells rapidly become more globular and less columnar.

Malignant adenoma or *adenocarcinoma* begins as a proliferation of the glandular tubules. The cells retain to a great extent their usual shape and regular arrangement. Further away from the original focus the glandular conformation becomes less and less marked, until it may completely disappear and be replaced by the usual carcinomatous picture.

Colloid cancer may be localized or, what is more common, diffuse. The mucosa and submucosa may be markedly infiltrated and the surface covered by a gelatinous material. This is better seen deeper in the tissues, as that exposed is dissolved by the gastric juices. On section a yellowish gelatinous material escapes. The cells are cylindric and there is a myxomatous degeneration of them and of the intercellular elements.

Squamous epithelioma occurs at the cardiac end of the stomach in connection with involvement of the esophagus. Is very rare.

Results of Cancer of the Stomach.—The involvement generally takes place within the gastric tubules. This is soon followed by an infiltration of the submucosa, the muscularis, and finally the serous covering, upon which there appear nodules. Perforation of the wall may then occur with subsequent involvement of the peritoneum; this is especially so in colloid cancer. Neighboring organs, as the liver, pancreas, and colon, may be affected by contiguity. If adhesions have formed perforation may be prevented and the neighboring tissues protected. Fistulous tracts may be opened between the stomach and duodenum or transverse colon, or with the pleura. Metastases may take place first in the neighboring lymphatics and then in more distant tissue, or secondary nodules may follow the entrance of tumor cells into veins. These are commonly carried to the liver, where they lodge and grow. The metastatic growths may be so large as to conceal the primary neoplasm. If at the pylorus there will be all the symptoms of obstruction, such as retention of food with decomposition.

Lactic acid fermentation is particularly common, as there is generally a lack of hydrochloric acid secretion. The stomach may become enormously dilated.

Following the ulcerative processes there may be extensive hemorrhage from the opening of a blood-vessel or there may be merely an oozing with the presence of the "coffee grounds" vomit.

Foreign bodies of many kinds may be found, either accidentally or intentionally swallowed. Intestinal parasites may also be present.

DISEASES OF THE INTESTINES

Malformations.—Complete absence may occur, but incomplete development is more common. There may be stenosis anywhere. The rectum may end in a blind sac, atresia ani, either low down or up in the sigmoid flexure. *Cloaca* formation refers to a condition in which there may be one common cavity acting as an outlet for the rectum and genito-urinary tracts. *Diverticula*, localized dilatations, are quite frequent, particularly *Meckel's diverticulum*. This is found in the ileum about three feet above the ileocecal valve. It is a finger-like projection of the same histologic formation as the intestine; is the remains of the omphalo-mesenteric duct. It may be adherent at the umbilicus, remain open, and allow feces to escape. *Enterocysts* are dilatations of the omphalo-mesenteric duct. There may be a *transposition* of the intestines, the colon ascending on the left and descending on the right. There is frequently an *abnormal* course of the large intestine, particularly of the transverse colon. This, instead of going directly across the upper part of the abdomen, takes a V-shaped course, the apex of the curve frequently extending as low as the pubes.

Hernia of the intestines refers to the abnormal entrance into or the passage through an opening.

Herniæ may be due to a weakening of the abdominal walls or to the failure of a canal to close. The mesentery may be longer than usual and allow very free motion, or there may be an abnormal amount of fat, causing an increase of weight.

The exciting cause in most cases is sudden exertion, or it may be the result of repeated strains.

Herniæ may be *external* or *internal*, *congenital* or *acquired*.

External are those in which the hernial sac lies outside of the abdomen. *Internal* are those in which the sac lies within one of the cavities within the body.

External	Internal
Inguinal.	Winslowian.
Femoral.	Mesenteric.
Umbilical.	Omental.
Obturator.	Diaphragmatic.
Ischiatic.	Retroperitoneal.
Labial.	
Perineal.	

The sac may contain only a portion of the small intestine or there may be some of the large abdominal organs present. There is generally a constriction (neck) at the point where the sac passes from the peritoneal cavity; below is a dilated pouch The inner wall of the sac is composed of the peritoneum.

A hernia is *reducible* if it can be pushed back through the opening from which it escaped. If it cannot be returned it is an *irreducible* hernia. The reduction may be prevented by adhesions having formed at the neck of the sac, by the accumulation of fecal matter, by edema or other causes. There may be such a constriction at the neck as to interfere with the circulation, a *strangulated* hernia. This may result from the same conditions, in a more severe degree, as cause an irreducible hernia, or from the entrance of more viscera into the sac. It is followed by an extreme passive congestion, inflammation of neighboring tissues, and hemorrhage and gangrene. If the strangulation is relieved early before degenerative changes have set in, the intestine may resume its usual condition.

In old hernias a chronic inflammatory process may have gone on, with the formation of fibrous adhesions between the sac and neighboring coils of intestine. This is due to the circulatory disturbances resulting from the twisting or stretching of the vessels.

Obstruction of the intestine may be due to the presence of foreign bodies within its lumen, to fibrous adhesions and bands, to a twisting or volvulus, to intussusception or invagination, or as a result from the formation of cicatrices at the seat of ulcerations. If the obstruction has been a chronic one, there will probably be some *dilatation* of the intestine above the constricted area. The part below may become atrophic.

Volvulus is the twisting of the intestine resulting in obstruction. It may twist in its long axis, but usually a loop of intestine twists around its mesenteric attachment. It occurs where the mesentery is unusually long and lax. The most common seat is in the sigmoid flexure. In volvulus there is a consequent obstruction to the blood-supply, and if the condition is not rapidly remedied, thrombosis, edema, and gangrene ensue. Above the twist the intestine will be dilated, there will be passive congestion, and frequently ulceration with perforation. Sometimes adhesions may form with a neighboring loop of intestine and no peritonitis result.

Intussusception or invagination is a condition in which one part of the intestine slips into the lumen of an adjoining part, like a glove-finger. The outer covering is called the *intussuscipiens* or sheath; the inner portion, the *intussusceptum*. Is most frequent in young babies and most common near the ileocecal valve. It may be due to convulsive or to reverse peristalsis. In children there may be found at the post-mortem table numerous invaginations which probably occurred during the death agony and have no significance.

The ensheathed portion may be very short or it may extend many feet. As a result of the invagination peristalsis is increased and the tendency is for the intussusception to become greater and greater. As the intestine is invaginated the mesentery is taken with it and the circulation is interfered with. That is followed by congestion, edema, and inflammation; a result of which is the formation of adhesions rendering the displacement permanent. If the process has been more acute, obstruction with gangrene and peritonitis usually follow. Sometimes the invaginated portion may slough off,

be passed through the rectum, and the edges of the intestine unite without any peritonitis resulting. There may be merely a stenosis through which fluid contents can pass.

Occasionally the rectum may extrude from the anus—*prolapse*. It usually occurs as a result of strained defecation. Is generally very easily reduced, but is likely to recur, as the sphincter muscle is usually weak. If allowed to remain, the prolapsed portion becomes inflamed, the mucous surface ulcerated, and necrosis may occur, as a result of acute strangulation by constriction of the sphincter.

Stenosis or narrowing of the lumen sometimes occurs, usually as a result of the contraction of cicatrices formed after ulceration. The primary ulcer may be syphilitic, tubercular, or rarely typhoidal.

The *syphilitic* ulcer has its long diameter at right angles to the long axis of the intestine and is generally completely annular. It is characterized by extensive fibrous tissue formation which, subsequently contracting, causes stenosis. The *tubercular* form lies transverse to the intestine, but does not completely encircle the gut. Constriction may occur as a result. The *typhoid* ulcer has its long axis parallel to that of the intestine and does not tend to form much fibrous tissue. If there is a cicatrix formed, there is usually merely a puckering of the intestine.

Stenosis may result from the presence of a neoplasm within the intestine or from pressure from without.

Dilatation results from incomplete obstruction. Is most marked in the large intestine as a result of retained fecal matter which undergoes decomposition and assists in the dilatation. This condition is usually associated with localized pouches or diverticula. Are most common in the rectum.

Perforation may be due to traumatism or may result from ulceration. If the opening is a small one, it may be filled up by a plug of fibrin and no damage result; if larger, there will be an escape of fecal contents into the peritoneum, with fatal results. If the process of ulceration has been a very slow one, as in tuberculosis, such dense adhesions may have formed as to prevent the escape of fecal contents into the abdominal

cavity. Instead of opening within the body the perforation may open out onto the skin surface, giving rise to a fecal fistula.

Rupture may follow injuries of the abdomen or may result from accumulations of gas.

Circulatory Disorders.—*Acute congestion* may result from active irritation or as the early stage of inflammation.

Passive congestion is common in diseases of the liver associated with engorgement of the portal veins, and to a less degree in chronic heart and lung disturbances. Local congestion is the result of some limited involvement of the mesenteric veins. The veins are swollen and prominent, the mucosa is swollen, edematous, dark bluish in color, and small petechial hemorrhages may be present.

Minute hemorrhages may occur in chronic passive congestion and in hemorrhagic diatheses. Severe hemorrhage may follow ulcerations of all kinds, particularly from the typhoidal, or wounds, such as the bites of intestinal parasites.

Edema is present in chronic passive congestion, and in inflammations, particularly if severe.

Embolism and **thrombosis** may occur. As a rule, there are no bad results, as the anastomoses are so extensive that necrosis does not occur. It may, however, be followed by *hemorrhagic infarction* with fatal necrosis of the portion of the intestine involved. The formation of the duodenal ulcer in burns is thought by some to be due to thrombosis.

Amyloid degeneration beginning in the fibrous wall of the small blood-vessels of the mucosa and submucosa is quite frequently met.

Pigmentary infiltration is often met in old people. The muscularis is filled with a yellow pigment that does not contain iron.

Hemorrhoids are varicose veins of the rectum. They may be either internal or external in character according to their relation to the sphincter ani. Are commonly the result of interference with the venous circulation. They may be due to cirrhosis of the liver, pressure from tumors, or from chronic constipation. The feces not only press upon the veins but

also give rise to a chronic proctitis that weakens the vessel walls. The hemorrhoids appear as small, dark bluish projections which on section are found to be formed of dilated veins, between which is usually a formation of fibrous tissue. The cavity may occasionally become filled with fibrin and be converted into a fibrous mass. Hemorrhage frequently accompanies hemorrhoids, and infection with inflammation is also common.

Inflammation of the intestine, or **enteritis,** may affect either the small or the large intestine or any portion of them. The mucosa and the submucosa are generally involved. If there is involvement of the stomach as well, the condition is known as *gastro-enteritis*.

The inflammation may be caused by the presence of irritating substances within the gut, as indigestible materials or poisons of various kinds. It may also be due to the presence of certain organic bodies resulting from imperfect digestion and fermentation.

Among the commonest causes of enteritis are the bacteria, such as the typhoid, cholera, and colon organisms. The intestinal parasites, particularly the Amœba coli, can occasion extensive inflammation.

Catarrhal enteritis may occur in any portion of the intestine. There is usually a slight congestion with some swelling. The lymphoid follicles are enlarged, there is considerable serous exudation, and occasionally small ulcerations. There is increased peristalsis on account of the inflammation and the intestinal contents are fluid as a result of the exudation. Shreds of epithelium may be discharged. In the intestinal wall there is a round-cell infiltration of the mucosa, the lymphoid tissue is increased, and there is an abnormal number of goblet cells.

Follicular enteritis is frequently a sequel to the catarrhal form. In it there is marked involvement of the solitary lymphoid follicles. They are much swollen, project from the mucous membrane, and sometimes undergo suppuration with the formation of ulcers. Is probably due to infection.

Suppurative enteritis is characterized by the exudation of

slight swelling and minute erosions of the mucosa. The muscular and serous coats will show slight infiltration and the lumen will contain epithelial and pus cells. In the *necrotic* or *gangrenous* variety the inflammatory processes are destructive. The mucosa is destroyed and the muscular and serous layers are soon attacked. The inflammation involves neighboring surfaces and a fibrinous peritonitis develops. This may be local, and by giving rise to adhesions between adjacent tissues no further extension takes place. The process may be very rapid and perforation follow before any restricting adhesions form; this is accompanied by a general and frequently fatal peritonitis.

In *interstitial* appendicitis there is a tendency toward excessive connective-tissue formation and it generally terminates as a chronic thickening.

Appendicitis may recover spontaneously with nothing more than a slight thickening of the walls or obliteration of the lumen. Adhesions may form, and by interfering with the surrounding organs give rise to various disturbances. The appendix may rupture with local or general peritonitis or there may form a localized abscess.

Colitis, inflammation of the colon, may be restricted to some one part of the colon, as the cecum, sigmoid flexure, etc., or involve all portions. It is generally due to the retention of large masses of hard feces, or to some of the infections, as tuberculosis and syphilis. Certain poisons, particularly the metallic, can set up severe inflammations; can also be due to products elaborated within the body, as in chronic nephritis. The mucosa is much thickened and there is a marked secretion of mucus. The mucosa frequently ulcerates and may become covered by a pseudo-membranous substance made up of desquamated epithelium and mucus. This may be passed from the rectum, in mass or as a cast (*mucous colitis*).

Proctitis, or inflammation of the rectum, may be due to the presence of masses of hard feces, of foreign bodies, or to infections, as tuberculosis, syphilis, and gonorrhea. If acute in onset, it however soon becomes chronic.

The mucous membrane is swollen, edematous, and minute

hemorrhages are frequent. Ulcerations of varying degrees of severity are present and may give rise to a *periproctitis* and *perirectal* abscesses. These may rupture externally and leave a fistulous tract opening both internally and externally; is known as *fistula in ano.*

INFECTIOUS DISEASES

Dysentery indicates an inflammatory condition of the colon and rectum characterized by ulcerations of the mucosa and the passage of numerous small, mucous, and bloody stools. It is a term that is applied to disturbances brought about by several causes. It is most common in tropic and semi-tropic, but occurs in the temperate zones as well.

It may be due to the presence of the Amœba coli, to the Shiga bacillus, or to various ferments and toxins of decomposing meat; sometimes it may follow the ingestion of poisons, particularly mercury.

In the mild or *catarrhal* forms there is congestion and edema of the mucosa with some petechiæ. There is a slight increase in the secretion, and ulcerations may be found involving the solitary follicles.

The *ulcerative* or *amebic* variety is much more severe. There is at first a marked nodular swelling of the mucosa. The mucous membrane at these points becomes necrotic and is cast off, exposing the infiltrated submucosa, which eventually sloughs off. The resulting ulcers vary greatly in size and shape, but are all characterized by having a decidedly undermined edge. Several ulcers may have communications beneath the mucosa and the ulcerations may extend to the serous covering. The amebæ will be found in the lesions. The process tends to become chronic, and for a long time the amebæ may be found in the stools, which also contain large amounts of pus.

As the inflammation subsides the ulcerations begin to cicatrize and recovery takes place. There is usually quite extensive atrophy of the mucosa and sometimes distortions due to contraction of the healed ulcers.

The most common complication is abscess of the liver, which in amebic dysentery is usually single.

There may secondarily result a *diphtheritic* dysentery; a variety in which there is formed a pseudo-membrane which occurs in varying extent. There may be numerous small areas so covered, or the entire colon and rectum may be in-

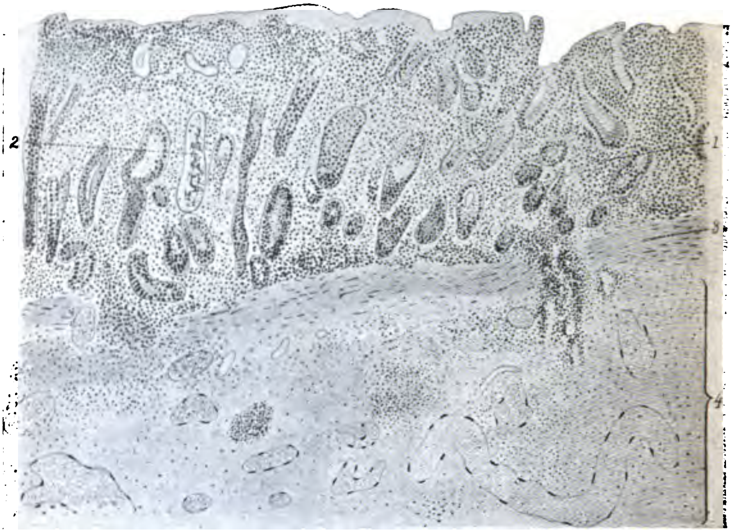

FIG. 135.—DYSENTERY OF LARGE INTESTINE. ×50 (Dürck).

The superficial layers of the mucosa are necrotic. In the deeper layers between the glands many leukocytes have accumulated (1); 2, fibrinous thrombus in a small artery; 3, muscularis mucosæ ruptured in many places by leukocytic accumulations; 4, submucosa with greatly dilated blood-vessels.

volved. If the process is mild, the mucous membrane is alone affected; but if severe, the submucosa may be destroyed.

The *bacterial* form of dysentery is, as a rule, much less severe in its manifestations than the amebic or tropical.

As a result of dysentery there is a chronic thickening of the

large intestine, and rarely perforation occurs. Abscesses of the liver result from embolism.

Asiatic cholera is an acute specific inflammation of the small and large intestines due to the comma bacillus or vibrio.

The post-mortem appearances differ according to the time at which death occurred. Early in the disease, in the algid form, the intestine is rose-red or purple in color, the mucosa shows numerous petechial hemorrhages, and its surface is covered by a transparent layer of sticky fibrin. The contents of the intestine are thin, watery, and cloudy, and very copious. In it are many small flakes of desquamated epithelium which give rise to the "rice-water" appearance that is characteristic of the condition. The discharges are alkaline, have but little odor, and although some blood may be present, bile is seldom found. In this early stage the solitary and agminated lymph-follicles are enlarged and frequently undergo ulceration. The large intestine is generally hyperemic, but otherwise negative.

In later cases, after the algid stage has disappeared, the intestine is no longer reddish in color, and is nearly empty, except for the presence of a foul-smelling gas. At this period an enteritis with the formation of a pseudo-membrane frequently occurs. This is a result of the coagulation necrosis of the mucous membrane, particularly of the tips of the villi.

The Peyer's patches are pigmented and bile may be found in the intestinal contents. The lesions are most marked in the lower portion of the small intestine, in which respect cholera differs from dysentery and poisoning by the metallic salts, which involve the large intestine.

In some cases there may be a hemorrhagic gastritis or an ulcerative colitis.

In a person dying from cholera there will be hyperemia of the pia, hyperemia and parenchymatous degeneration of the kidney, and bronchopneumonia. The liver and spleen will be smaller than usual.

Early in the course of the disease the bacillus is present in the intestinal contents in great number, in a pure culture.

Typhoid fever is an acute infectious fever caused by the

FIG. 136.—ILEUM; TYPHOID FEVER (EARLY STAGE) (Nicholls).

Peyer's patches and solitary follicles greatly swollen; superficial ulceration.

B. typhosus, and its characteristic lesion is ulceration of the lymphoid tissue of the small intestine, particularly the Peyer's patches. The upper part of the colon is also generally involved.

The lesions in the intestine correspond closely to the clinical course of the disease and indicate by their appearance the duration of the infection. The organisms gain entrance into the individual through the mouth in food, or more commonly in the water. They pass to the small intestine and there give rise to the various lesions. At first the mucous membrane becomes hyperemic and swollen, the solitary follicles and the Peyer's patches become larger, their surfaces irregular and hyperemic. In the course of a few days they fade and become quite pale or grayish-white as necrosis begins. The Peyer's patch is elevated and sharply defined from the neighboring mucosa. Microscopically the intestinal wall presents a high-grade round-cell infiltration and an increase in epithelioid cells. During the second week there is a necrosis of the hyperplastic lymphoid nodes. The tissue is cast off in shreds. The greater part of the follicle may be sloughed off, leaving a long, irregular ulcer with a smooth floor lying parallel to the long axis of the intestine. The ulcers usually appear toward the end

of the second week of the disease. They extend to varying depths; in some cases involving the lymphoid tissue alone, but at times the necrosis passes on to the submucosa and even to the serous covering. Perforation is common. Ulceration is most marked in the small intestine near the ileocecal valve.

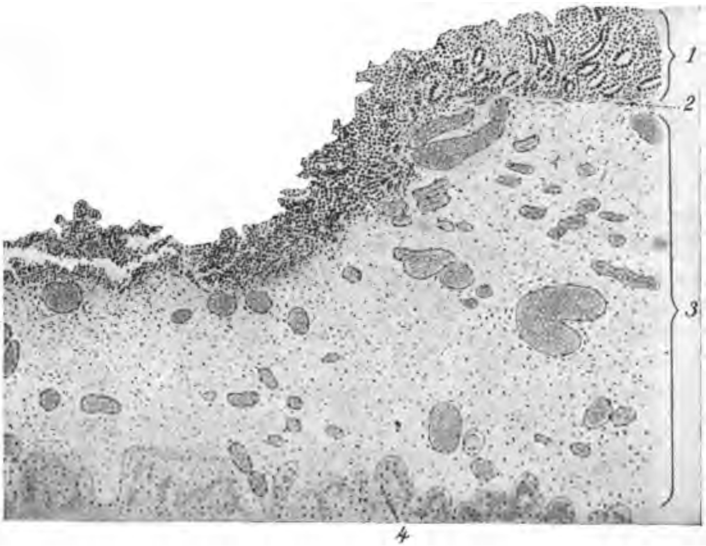

FIG. 137.—TYPHOID ULCER AFTER DETACHMENT OF SLOUGH. ×50 (Dürck).

The margins of the defect end abruptly; in the floor of the ulcer, which reaches into the submucosa, are seen a few necrotic portions of tissue with extensive infiltration of leukocytes. 1, Mucosa; 2, muscularis mucosæ; 3, submucosa with overfilled blood-vessels; 4, muscularis.

By the end of the third week the necrosis and ulceration ceases and reparative processes begin. The hyperplastic lymphoid tissue resumes its normal condition by disintegration and absorption of the newly formed cells. The ulcerated surfaces heal by cicatrization and by extensions from the surrounding mucous membrane.

The increase in the cellular elements in the lymph-nodes is the result of the proliferation of the endothelial cells of the lymphatic spaces, blood-capillaries, and reticulum of the lymphoid tissue. It is brought about by the action of a toxin. These cells give rise to necrosis in the lymph-nodes, liver, and spleen by thrombosis which interferes with the blood-supply. They may be found in the lung.

The *complications* of typhoid fever are several, but the most serious are *hemorrhage* and *perforation.* Small hemorrhages may be the result of oozing from the ulcerated surfaces. Its presence causes the stools to be dark brown in color. Severe hemorrhage follows the destruction of the walls of some larger vessel. It may remain in the intestine long enough to undergo changes and give rise to the "tarry stools." Occasionally the loss may be so sudden and large that the blood is discharged when still bright in color. Perforation follows extensive ulceration, and may occur by the end of the second week, but usually later during the third. The intestinal wall may have become so thin that solid substances may lacerate it and escape into the peritoneal cavity. If the process has been comparatively slow, adhesions may have formed so as to prevent a general infection. If this has not happened, general purulent peritonitis, nearly always fatal, will be set up.

The mesenteric lymph-nodes become enlarged, soft, and hyperemic. As the processes within the intestine increase in severity these nodes show fatty metamorphosis, softening, and even necrosis. The spleen becomes much larger, soft and flabby, and hyperemic. Sometimes it will be the seat of infarctions and abscesses. The muscles, particularly the recti, show Zenker's degeneration, a hyaline change. Minute hemorrhages may also be present in the muscles. The heart muscle undergoes a certain amount of cloudy swelling and at times is the seat of acute myocarditis. Acute endocarditis occasionally occurs, but is not as common as in other infectious diseases. There is no leukocytosis present unless pneumonic inflammations have arisen; acute broncho-pneumonia and croupous pneumonia are quite common com-

plications. The kidneys are quite commonly the seat of acute parenchymatous nephritis and areas of focal necrosis are also frequently observed. Hemorrhagic areas may be found.

The bacilli are present not only in the intestine but elsewhere. Early in the disease they can be readily obtained from the blood. They are found in the skin lesions, the "rose spots," also in the urine. The internal structures, as the spleen, mesenteric nodes, and gall-bladder, contain them. The organisms may remain within the body for a long time after convalescence and then give rise to suppuration, as ostitis, parotitis, and meningitis.

Pulmonary tuberculosis is a not uncommon condition occurring after the patient has apparently entirely recovered.

An important test in the making of the diagnosis of typhoid fever is the *Widal reaction.* It is based upon the principle that when the blood of a patient suffering from typhoid fever is added to a fresh culture of the typhoid organism the bacilli will gather into clusters and gradually lose their motility, a process known as "clumping." The reaction is performed as follows: The most satisfactory way is to obtain the blood in a fresh state, and if one can get a sufficient amount to allow the use of the serum alone, it is even better. A drop of blood or serum is forced out of a capillary tube, in which it should be received, and to this nine drops of sterile water are added. This is thoroughly mixed, and one drop of this mixture added to one of the culture gives a dilution of 1:20. The culture to be used that is generally recommended is a bouillon one not more than twenty-four hours old. Some authors recommend a fresh agar culture, but there is danger of the bacilli being already clumped to some degree. Dilutions of 1:10 and 1 : 50 should also be employed as control tests. A drop of this solution is placed on a cover-glass, which is then inverted over a hollow-ground slide. The reaction is said to be positive if within forty-five minutes the bacilli are found to be gathered in little groups and their motility almost or entirely absent.

If the blood cannot be sent fluid, several drops of blood

should be placed on a sterile slide and when dry sent to the laboratory. One of the drops is dissolved in a drop of sterile water and then diluted till the proportion is one to fifty. The rest of the technic is the same as with the fluid blood.

This reaction, although generally seen within forty-eight hours after the onset of the disease, may be delayed till much later. It may also appear in those who have suffered from typhoid fever some time previously.

Paratyphoid fever presents lesions that differ somewhat from typhoid. There are not the characteristic intestinal

FIG. 138.—TUBERCULAR ULCERATION OF THE INTESTINE (Stengel).

changes. The clinical appearance may be similar, but there may be no ulcerations present in the intestine or else the ulcers may be very irregular and not typical. Two strains of organisms very closely related to each other, but differing in certain respects in their cultural characteristics from the typhoid bacillus, have been isolated.

Tuberculosis of the intestine is common in children as a primary infection; in adults it is frequently secondary to pulmonary and laryngeal tuberculosis. In children the

source of infection is probably tubercular milk. The consensus of opinion at present is that the tubercle bacillus found in the milk of diseased cows is quite capable of infecting the human organism. The infection in adults is generally due to the swallowing of sputum.

The lymphoid tissue in the lower portion of the ileum is the usual seat of the primary lesion. There is the formation of a tubercle with coagulation necrosis; the central portion is cast off and an ulcer with thickened edges and a yellowish base is formed. Several ulcers become confluent and a large irregular one results. Instead of remaining the shape of the Peyer's patch, the ulcer tends to increase in size laterally, unlike the typhoid lesion. This is due to the extension by means of the lymphatics which surround the intestines. The lesion usually involves the submucosa as well as the mucosa, also the muscularis and sometimes the serous coat. As a rule, the peritoneal covering at the site of the ulcer is the seat of numerous small tubercles in clusters. There may also be found white lines connecting neighboring tubercles; these are probably lymph-vessels that are stopped up by caseous matter.

Perforation is the most dangerous complication, but it does not frequently occur, on account of adhesions that have been formed during the progress of the disease. Tubercular peritonitis may result from tuberculosis of the intestine. The ulcers may be present in all stages, some completely healed while others are undergoing active changes. As a result of the position of the ulcer the cicatrization is more likely to be followed by stenosis than is the case in typhoid fever. The mesenteric nodes are usually involved and at times may show much more marked disease than is seen within the intestine.

Syphilis of the intestine is seldom met with, and when seen usually appears in the rectum. The small intestine may be involved in cases of congenital syphilis. Small gummata are seen which show a marked tendency to undergo softening and ulceration; the lymphoid tissue being generally the site of the lesions. The rectal form is usually the result

of direct infection and the disease may appear as the primary chancre, as papules and mucous patches in the secondary stage, and as gummata in the tertiary. In the third stage there may be such extensive ulceration as to destroy the mucous membrane almost completely for several inches along the bowel. The wall of the intestine at the seat of ulceration may become much thickened by a round-cell infiltration. Following this extensive ulceration, cicatrization with contraction and stenosis may occur.

Actinomycosis and **leprosy** very rarely appear. **Anthrax** sometimes involves the small intestine. Is found in wool-sorters, brush-makers, and others exposed to infection. The mucosa and submucosa show hyperemia and a hemorrhagic edema, and extensive ulceration appears. The tissues are dark colored and necrotic and the ulcers are surrounded by a zone of hemorrhagic infiltration. The adjacent lymph-nodes and the spleen are enlarged; and the anthrax bacillus can be found in greatest numbers in the locality of the necrosis.

Enteromycosis refers to a condition in which there is an infection of the intestine by the eating of decayed proteid substances, as putrid meat, fish, sausages, and so on. Sometimes occurs in epidemics. The intestinal lesions vary from a mild catarrhal enteritis to a pseudo-membranous inflammation and ulceration. Is accompanied by diarrhea and depression. The symptoms, both constitutional and local, probably depend upon the action of toxins elborated in the decaying matter rather than upon the bacteria themselves.

Tumors.—*Connective-tissue* growths are unusual and generally benign. Fibroma, lipoma, and myxoma are sometimes seen. They may cause some obstruction if large. *Sarcoma* is rare. It arises within the submucosa and extends very rapidly, elevating the mucosa. Is generally round-cell in character and may with difficulty be distinguished from the lymphatic enlargements that are present in the intestine in leukemia and Hodgkin's disease.

Epithelial tumors are more common and not infrequently cause death. *Adenomata* are quite common, and may be

diffuse or of a polypoid nature. They originate from the crypts of Lieberkühn, as a rule. The polypoid form is more common in the rectum and may undergo inflammatory changes as a result of injury by the feces.

Carcinoma is the most common of the intestinal tumors and is usually composed of cylindric cells. It is most frequent at certain sites, as the papilla of the common bile-duct, the ileocecal valve, the hepatic, splenic, or sigmoid flexures, and within the rectum. It is somewhat elevated, its surface rough, irregular, and ulcerated, and it involves the entire lumen of the gut, causing obstruction. Bleeding from the ulcerated surface is quite common. If the connective-tissue stroma predominates the growth is hard and firm; if very cellular, it is soft, whitish, and spongy. These tumors show a marked tendency to undergo mucoid and colloid degenerations, and metastases to the neighboring lymph-nodes and liver are common.

Squamous epithelioma originate at the anus and may involve neighboring structures.

Parasites of both animal and vegetable types are common occupants of the intestine. Of the *animal parasites*, the round worms, as the Ascaris lumbricoides, Oxyuris vermicularis, Trichocephalus dispar, Anguillula intestinalis and stercoralis, and Eustrongylus gigas; the tape-worms, Tænia solium, T. saginata, T. echinococcus, and Dibothriocephalus latus; and the sucking-worms, the Uncinaria, are found present under various circumstances.

Other and more unusual forms are the Cercomonas, Trichomonas, Balantidium coli, and the Amœba coli.

Foreign bodies of innumerable varieties have been swallowed and subsequently found within the intestine. Sometimes dense masses of fecal concretions, enteroliths, are found. These are composed of a nucleus of epithelium, hair, or other foreign bodies, surrounded by dried fecal matter. They may give rise to local irritation. In the lower animals they are of large size, but in man are generally small.

Tympanites or *meteorism* is a condition of dilatation of the intestine by the presence of a large amount of gas. It may

be so severe as to cause a paralysis of the muscular coat with a cessation of peristalsis.

DISEASES OF THE LIVER

Malformations are not common and seldom of importance. Complete absence is seen in acardiac monsters. Variations in the number of lobes and in the fissures may occur. Portions of hepatic tissue may be separated from the main mass, but are usually connected by a pedicle of connective tissue. Malformations may be acquired particularly as a result of tight lacing, which causes a deep transverse notch upon the anterior surface which may almost divide the organ, the hepatic tissue along the line of pressure undergoing atrophy.

The position of the liver may be changed by relaxation of its ligaments or by pressure from tumors within the abdomen.

The ribs posteriorly and the right crus of the diaphragm may by pressure form long furrows.

Disturbances of Circulation.—The liver is peculiar in its blood-supply in that it contains two systems. One of these, the lesser, supplies nutrition to the stroma; the other, which is of much greater importance, supplies the blood necessary for the carrrying on of the hepatic functions. This latter, the portal system, divides into many branches that ramify throughout the acini and empty into the central veins of the lobules, branches of the hepatic. The blood flows very slowly through the organ and is under very little pressure, consequently is readily interfered with by slight obstruction.

Anemia may be part of a general anemia or may be due to pressure upon the blood-vessels. The organ is pale, but may vary in color according to the amount of bile or of fatty degeneration present.

Active hyperemia occurs normally during digestion, and is also present as an accompaniment of inflammation, in which case the areas are circumscribed. May be general as a part of an infectious process. The organ is slightly enlarged, softer, dark red in color, and on section blood readily escapes.

Passive hyperemia is of greater pathologic importance than the active. It is caused by interference with the escape of the blood into the vena cava. Is found in valvular diseases of the heart, in those conditions interfering with the pulmonary circulation, as emphysema, chronic fibroid

FIG. 139.—NUTMEG LIVER: CHRONIC CONGESTION DUE TO CARDIAC DISEASE (Bollinger).

phthisis, etc., and to pressure upon the vena cava by tumors. Pleural effusions with adhesions may cause it.

As a result of the obstruction to the circulation the central vein of the lobule first becomes dilated, and subsequently the capillaries in communication. Following this continued

pressure there is atrophy of the cells in the central zone and at times even of those as far out as the periphery of the lobule.

The organ is at first enlarged, the anterior edge rounded, and may be darker in color. On section is seen the characteristic reddish-brown and yellow mottling known as the "nutmeg liver." The reddish-brown areas represent the deeply congested portion surrounding the central vein, while the yellow indicate a fatty degeneration and infiltration of the peripheral cells. In between these two zones there is a less marked area in which the cells are atrophic and contain dark-brown pigment.

If the congestion has been present for a long time the organ may become smaller on account of atrophy of the hepatic cells. The surface of the liver becomes uneven, due to hyperplasia of connective tissue, and is darkly pigmented, a condition known as *cyanotic induration.*

In some cases there is a deposit of hematogenous pigment throughout the organ, causing it to be dark red. Such a change is spoken of as *red atrophy*, as the liver is smaller than normal.

As a result of chronic congestion the action of the liver may be much interfered with, one of the most common symptoms being slight jaundice, probably due to the obstruction of the bile-ducts and capillaries by the swollen endothelial cells. The bile is also generally more viscid than normal.

Embolism and *thrombosis* not infrequently occur and cause greater or less disturbances according to their location and magnitude. As a rule, no serious conditions arise, as the collateral circulation is so extensive. The hepatic artery is capable of supplying sufficient blood for both the nutrition and function of the organ, so that marked interference with the portal circulation does not necessarily result seriously. If the portal vein is completely obstructed, the secretion of bile stops, the blood is retained in the portal system, and death may result. If the hepatic artery is obstructed the liver rapidly becomes necrotic.

Numerous small foci of necrosis may result from infectious emboli in the portal capillaries. Is known as *focal necrosis*

and is seen in puerperal fever, and in septic conditions involving the portal system, also in various infectious diseases. These foci differ in color from red to yellow according to whether blood or fat is present in the greater amount. The interlobular portal vessels are frequently the seat of a hyaline thrombosis.

Infarctions of the liver, either hemorrhagic or anemic, are almost unknown, as the anastomoses of the hepatic vessels are so extensive.

Hemorrhage of the liver occurs in severe infections and intoxications.

INFILTRATION AND DEGENERATION

Pigmentation of the liver may be *hematogenous*. The blood coloring-matter may not be completely transformed into bile-pigment and is deposited in the interlobular tissues, in the peripheral zones, and in the central area of the lobule. This occurs to some degree in nearly all diseases of the liver. Is marked in chronic congestion, amyloid disease, cirrhosis, and pernicious anemia. The pigment is found as dark brown granules, is probably hemosiderin, as its gives the iron reaction a blue color when pure sulphuric acid and potassium ferrocyanid are added.

Biliary pigment due to the retention of bile is not uncommon. The liver becomes dark yellowish-green, at times almost black in color. Is most marked in the central zone of the liver lobules.

Pigment in the form of melanin resulting from blood destruction in chronic malaria, and also as anthracotic particles, is found occasionally.

Fatty infiltration is to a certain extent normal, is more marked the younger the individual. After a meal, particularly if rich in fat, there is an infiltration in the peripheral zones. This is soon removed if the hepatic functions are being carried on normally. If the oxidation does not take place properly the fatty infiltration may become of an extremely high grade. Is best seen in chronic tuberculosis, particularly if forced feeding has been indulged in; in

marasmatic individuals and in alcoholics, especially when malt liquors have been consumed to excess.

The liver becomes much enlarged, is at times nearly twice its normal size; the edges are rounded, its color is a uniform yellow, and it is doughy, slight pressure causing an indentation. On section the knife will be covered with small droplets of fat. The center of the acini may be darker than the periphery on account of congestion. The cells, microscopically, are seen to contain comparatively large droplets of fats which show a marked tendency to coalesce and form one large drop which may greatly distend the cell and push aside its nucleus, giving rise to the "signet-ring" appearance. The infiltration begins in the periphery and extends inward. On account of the distention of the cells the blood-vessels may be hidden from view and so obstructed as to give rise to considerable anemia and diminishment of functional activity.

The cells in this condition do not appear to be much damaged and are apparently able to resume their work when the fat disappears.

Parenchymatous degeneration or cloudy swelling occurs in most of the infectious fevers and in intoxications. The liver is somewhat enlarged and grayish-yellow in color. Microscopically the cells are seen to be swollen and filled with albuminous particles which obscure the nucleus. The organ readily recovers if the exciting cause passes away, otherwise fatty degeneration will ensue.

Fatty degeneration or metamorphosis occurs in severe anemias, in phosphorous and arsenic poisoning, and in certain of the infections, as yellow fever. The liver is smaller than normal, yellow in color, and soft. Oil drops exude from the cut surface. Microscopically the cells are seen to contain numerous minute fat granules that do not, as a rule, tend to coalesce. Is most marked in *acute yellow atrophy* of the liver. In it the liver is greatly decreased in size, the edges thin, its color uniformly yellowish or streaked with brown, and is very soft, so much so that it may not retain its shape. The capsule is much wrinkled. On section the tissue in many places seems almost liquid while elsewhere it is firmer

and darker in color. Oil fairly drips from the surface. Microscopically the cells are seen to have undergone extreme metamorphosis, and to have been replaced by pigment. The hepatic tissue may be completely destroyed to a great extent; the degenerated material is absorbed and the decrease in size results.

Occasionally bright red or dark red areas are present. These represent foci of hemorrhagic infiltration or pigmentation.

The causes of this condition are practically unknown. It is most common in young women. It appears in infectious fevers, particularly puerperal, in syphilis, in phosphorous poisoning, and again without any apparent cause. Microorganisms of many kinds have been found in the bile-vessels and in the hepatic tissue, but no specific one has been isolated. Some authors think it due to the absorption of toxins from the intestine.

The destruction apparently begins in the peripheral zone around the portal vessel and extends toward the center.

The urine contains leucin and tyrosin.

Amyloid degeneration of the liver results from long-continued suppuration, as in chronic tuberculosis, in suppurative bone diseases, and is usually accompanied by similar degeneration elsewhere. The liver is larger than normal, a little pale in color, and is quite firm. The cut surface frequently appears quite translucent and may be a grayish-white or a dull yellow color.

The degeneration begins in the wall of the capillaries, which become much thickened; so much so that the blood-supply may become obstructed. Pressure is also exerted upon the adjacent liver-cells, many of which undergo atrophy. The peripheral zone is the one in which the change is first noticed, and from there it extends toward the center of the lobule. The connective tissue is also involved and the affected areas may become very extensive. As the epithelium is involved secondarily the organ is able to carry on its function as long as a sufficiently large number of cells do not become atrophic.

Edema of the liver occurs in the course of long-continued

circulatory disturbances and in severe infections. The tissue is swollen and many of the cells may contain vacuoles.

Atrophy as a primary condition depending upon local anemia is rare. Is quite common as a secondary lesion, depending upon pressure, such as tight lacing, or that resulting from the contraction of cicatricial bands. The organ becomes irregularly atrophic, the cells in the involved areas are distorted, irregular, granular, and pigmented. The nuclei generally break down.

In *leukemia* there are collections of leukocytes in the connective tissue in between the lobules.

Acute interstitial inflammation of the liver usually follows upon acute infectious conditions elsewhere, particularly in the intestines, but may be due to trauma. Is always suppurative in character and may appear as a single large abscess or as numerous small ones. The exciting microorganism may gain a foothold in the liver by means of (1) the portal vein, (2) the hepatic artery, (3) the hepatic veins, (4) the umbilical vein in the new-born, (5) the bile-ducts.

The organisms lodging as emboli within the capillaries set up a focus of suppuration.

Infection from amebic dysentery generally gives rise to a single large abscess in the right lobe. The pus contained within such differs from that ordinarily found in that it is grayish or pinkish in color, and mucilaginous in consistency.

In bacillary dysentery numerous miliary suppurative foci are found.

In suppurative thrombophlebitis (pylephlebitis) the purulent process follows along the course of the infected vessels, where it can be seen in the form of soft, white lines of suppuration with inflammatory reaction in the adjoining tissue.

The liver-cells degenerate, lose their nuclei, and become necrotic. At the same time there is extensive round-cell infiltration within as well as around the lobules. Pus cells soon appear and a small focus of suppuration is formed. This process may continue until a large abscess results.

If the abscesses are small the organ may regain an approximately normal condition through absorption of the pus with

cicatrization. Large abscesses may very slowly become absorbed and their walls much thickened; lime salts may be deposited.

Instead of a favorable termination the abscess may rupture into the abdomen, into the thorax, or if adhesions have formed through the abdominal wall.

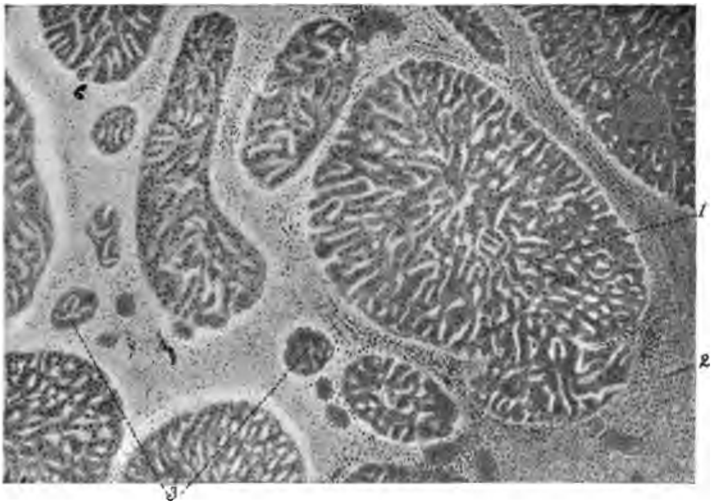

FIG. 140.—ATROPHIC CIRRHOSIS OF THE LIVER. × 40 (Dürck).

Well-marked bands of connective-tissue (2) divide the parenchyma of the liver into irregular islands of varying size; even in the larger of these there is no division into lobules (1). Vena centralis absent in some places; in others, excentric (upper right corner). 3. Smaller islands of liver cells. Scattered heaps of round cells in the connective tissue and toward the left a few epithelial canals with darkly colored nuclei (newly formed bile-ducts).

Chronic interstitial hepatitis is characterized by an overgrowth of fibrous connective tissue supposed to be due to the long-continued action of some mild irritant. Alcohol is thought to be the commonest cause.

The more usual form is that resulting from the irritating substance being conveyed in the blood, *hematogenous;* a

second and rare form is the *hepatogenous*, one in which the changes follow upon an obstruction to the bile-vessels.

Atrophic Cirrhosis (*Laennec's Cirrhosis*, "*Hob-nail*" *Liver*).—Is hematogenous in character, as in the majority of cases it is due to the presence in the circulation of a poisonous substance formed by distilled liquors. Early in the disease the organ may be somewhat enlarged, but in the typical stage the liver is small, contracted, the surface irregular, the color varying greatly, is very hard, dense, and cuts with great difficulty. The nodules that project are composed of liver-cells, while the depressed areas are formed by bands of connective tissue that have contracted. These bands are grayish in color, the elevated portions yellowish or brownish, the color depending upon the fatty degeneration or the presence of bile.

Microscopically the process begins as a localized infiltration of round cells about the interlobular branches of the portal vein. This is followed by a proliferation of the connective tissue with the formation of new fibers. These increase in number, and undergoing contraction interfere with the circulation. This gives rise to certain associated symptoms, as ascites, gastro-intestinal catarrh, hemorrhoids, and distention of the superficial abdominal veins (the caput medusæ). Jaundice is seldom present. The entire lobule eventually becomes surrounded, and as the contraction continues the hepatic cells undergo atrophy till at last there may be an island composed of a few epithelial elements. The connective tissue does not tend to become intralobular.

Associated with the above changes is more or less marked fatty degeneration. An important feature in this disease is the proliferation of bile-ducts in the interlobular connective tissue. There is usually a decided increase in their number.

Sometimes the liver-cells may contain large amounts of pigment granules, varying in shade from yellow to dark green; may be hemosiderin or bile-pigment.

Hypertrophic cirrhosis (*Hanot's cirrhosis*) derives its name from the fact of the liver being much larger than normal.

Its surface is smooth or finely granular, dense and firm, and cuts with difficulty, but not with so much as in the atrophic form. The cut surface shows usually a decidedly mottled appearance, areas of yellow, gray, and green being intermingled. The connective tissue is not seen in bands sur-

FIG. 141.—CHRONIC INDURATING CIRRHOSIS OF THE LIVER (McFarland). *a*, Liver lobule, most of whose cells are in a fatty infiltrated condition; *b*, greatly hypertrophied periportal connective tissue; *c*, proliferated bile-ducts.

rounding islands of liver-cells, but occurs in a diffuse arrangement. It does not tend to contract and interference with the portal circulation is unusual.

Microscopically the new-formed connective tissue is seen to extend into the lobules between the columns of cells as well as in the interlobular areas. The bile-ducts are increased

in number and many of them are seen to be obstructed by broken-down cells and pigment. Surrounding them is an increase of connective tissue, a periangiocholitis. The number of bile-ducts may be so great as to give rise to a condition resembling an adenoma or even a carcinoma.

On account of the obstruction to the ducts jaundice is present and the liver may be dark green in color.

Atrophic Cirrhosis. (Laennec's.)	Hypertrophic Cirrhosis. (Charcot's.)
Small. Surface uneven, pale.	Large. Surface smooth, mottled green.
Connective tissue surrounding acini.	Connective tissue generally diffused and extending into acini.
Ascites appears early and often severe.	Appears late if at all.
Jaundice rarely present.	Jaundice comes on early and is very marked.
Hemorrhoids common.	Unusual.

Biliary cirrhosis is a condition in which there has been an overgrowth of connective tissue as a result of obstruction of the large bile-ducts. The congestion of the bile in itself acts as an irritant, but there is usually an infection by micro-organisms from the intestine. The liver becomes swollen and inflammatory reactions appear. The surface is smooth and the tissue is deeply stained by the bile. The peripheral zones of the acini show small areas of necrosis which may become transformed into minute abscesses if bacteria are present. Instead of suppurating the necrotic areas may be replaced by connective tissue and give rise to widespread induration that closely resembles hypertrophic cirrhosis.

The bile-ducts may increase in number and evidences of regeneration of the hepatic cells are shown by the presence of mitotic figures.

This form generally follows obstruction of one of the larger hepatic ducts or of the common duct. If the ob-

struction has been complete, rapid fatty degeneration and acute atrophy may occur.

Perihepatitis or inflammation of the capsule of the liver may be present in cirrhosis and as a result of chronic peritonitis. The capsule may become greatly thickened and by contraction bring about atrophy of the hepatic tissue immediately underlying.

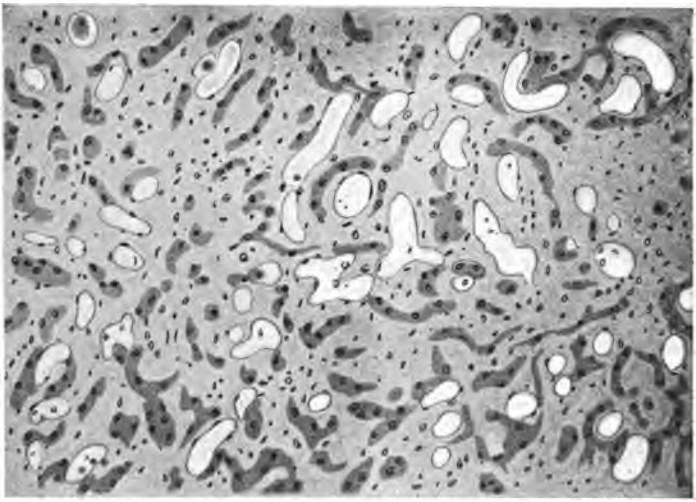

FIG. 142.—(HYPERTROPHIC) DIFFUSE CIRRHOSIS OF THE LIVER. × 160 (Dürck).

Lobular marking lost, the liver tissue separated into narrow strands by proliferating young connective tissue with short fibers, in which are wide capillaries with distinct endothelium.

Rupture of the liver usually results from direct injury. Is more commonly seen in the newly born when there has been instrumental interference.

INFECTIOUS DISEASES OF THE LIVER

Tuberculosis of the liver is secondary to lesions of the disease elsewhere and may have become infected through

either the blood or the lymph-channels. It appears generally as miliary tubercles scattered throughout the organ, or as larger necrotic foci.

Microscopically the lesions are the same typical ones as are found everywhere in the disease.

Rarely there is a single large cheesy focus.

Syphilis of the liver is a common involvement in that

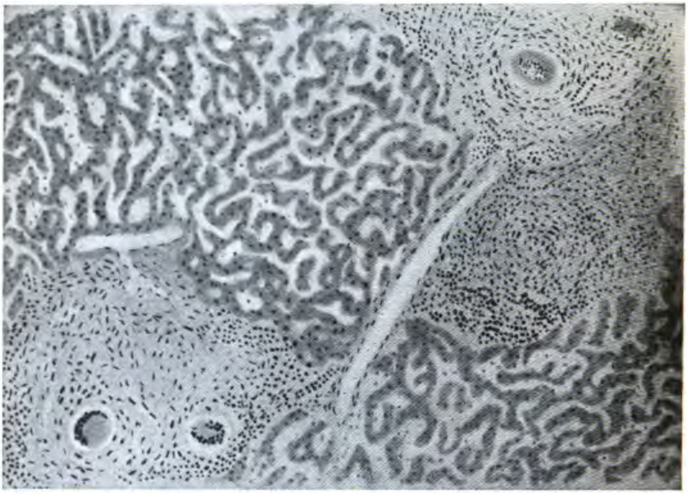

FIG. 143.—MILIARY TUBERCULOSIS OF THE LIVER. × 70 (Dürck).

Two foci, consisting of smaller confluent tubercles, which are still distinguishable. The giant cells are rounded. The foci are situated in the periportal tissue in the vicinity of a portal branch.

disease. In adults who have acquired syphilis there is frequently a diffuse proliferation of connective tissue with atrophy of the hepatic cells that closely resembles atrophic cirrhosis. Generally the disease manifests itself in the form of localized proliferations of connective tissue that divide the liver into numerous small but well-defined lobes. A certain area may become almost constricted off from the rest of the organs. The irregular distribution of the connective tissue is

the characteristic feature. This form probably originates as an inflammatory thickening about the portal veins and the bite-ducts.

Gumma may also be present in acquired or congenital syphilis, either singly or in numbers. In the acquired form the single ones are usually the larger. They occur as rounded yellowish masses, the center of the larger ones frequently being the seat of coagulation necrosis. Surrounding them is a zone of hyperemia and there is generally some connective-tissue hyperplasia. This occurs in the form of bands radiating from the center, giving a characteristic stellate appearance to the resulting scar.

Congenital syphilis of the liver may manifest itself in a diffuse form or as gummata. In the diffuse variety there is a widespread connective-tissue proliferation and round-cell infiltration. The organ is yellowish or brown, sometimes larger than normal, and extremely firm, almost like sole leather. The round-cell infiltration is found in the neighborhood of the blood-vessels, even being seen within the walls. The liver epithelium is frequently the seat of fatty degeneration, giving rise to the "acute yellow atrophy" of the liver of the new-born.

The congenital gummata are not, as a rule, circumscribed. They are found in the interlobular tissue and may be located within the wall of a blood-vessel or of a bile-duct.

Leprosy is sometimes found in the liver, where it occurs as granulomatous masses containing the characteristic giant cells and bacilli.

Actinomycosis rarely occurs in the liver. When present, it is generally due to secondary involvement by extension from the lung.

Tumors.—Primary growths of the liver are very unusual, but it is nearly always involved secondarily in malignant disease of other localities.

Angioma is about the most frequent new growth. It generally occurs upon the surface of the liver as small, circumscribed, dark red or purplish areas that may be single or multiple. Sometimes they may be as large as an orange.

They are more common in old, poorly nourished people. The surrounding liver tissue shows no changes. Microscopically the structure is that of a cavernous angioma.

Fibroma, *Lipoma*, and *Myoma* are very rarely met with.

Sarcoma may be primary or secondary, the latter being the more usual.

The primary variety is more frequently found in children. It develops from the connective tissue of the hilus or of the periportal tissue and appears either as a round-cell or a spindle-cell growth.

Secondary sarcoma follows as a hematogenous infection from a primary focus elsewhere, and is formed of the same variety of cells as the original growth. Melanotic growths are commonly secondary to sarcoma of the eye.

The liver is increased in size and is the seat of numerous rounded masses varying in size and pale in color.

Adenoma is found in livers that are otherwise normal, and also in cases of cirrhosis. May be single or multiple, nodular, somewhat encapsulated, and grayish or pinkish in color. At times it may be difficult to distinguish adenoma and cirrhosis from carcinoma both by the naked eye and by the microscope.

Hypernephroma, a variety of adenoma that develops from a misplaced fragment of adrenal tissue, is but rarely seen. The cells in this form are cubical and contain fat and pigments.

Carcinoma may be primary, which is uncommon, or secondary, which is the usual form.

Primary cancer may appear as a large, more or less circumscribed tumor, usually in the right lobe. It probably originates as an adenoma and extends into the surrounding tissues. Microscopically there are seen irregular cell nests surrounded by a well-marked connective-tissue framework. The cells resemble the liver parenchyma, as a rule, but in places they are smaller and more closely simulate the cells of the bile-ducts. Fatty degeneration and necrosis are common, and pigment, either biliary or melanotic, is not infrequently present.

Another variety of the primary growth occurs as a diffuse

carcinomatous infiltration with a general increase in the size of the organ. The surface of the liver is granular and nodular, and grayish or brownish in color. Larger circumscribed nodules may also be present. Except for the large nodules, the appearance of the organ is very similar to that in cirrhosis.

Microscopically it is seen that the entire tissue is infiltrated by the cancer cells. Surrounding these collections of cells are bands of connective tissue, and lying in between the two is a narrow zone composed of atrophic liver-cells that have been pushed aside by the neoplastic cells. The capillaries are found to be filled with cancer cells and the infiltration may become so great as to obliterate blood-vessels and bile-ducts and completely destroy the function of the liver.

A third variety of primary cancer is the interlobular form. In this the carcinoma has extended along the distribution of the portal vein and invades but slightly the neighboring tissue. The liver appears to the naked eye very much like an atrophic cirrhosis, having the same irregular surface. Is frequently spoken of as cirrhotic cancer.

Secondary cancer is frequently found in cases of primary growths of the stomach, intestine, pancreas, mammary gland, and uterus. Occurs in connection with those organs whose venous blood empties into the portal system. It generally appears in the form of numerous nodules disseminated through the organ. The nodes vary greatly in size, the large ones frequently showing a depressed, umbilicated center, the result of necrosis and softening with absorption. These secondary growths are, as a rule, quite well circumscribed. The cells that compose them resemble more or less closely those of the original neoplasm. Masses of these cells gain entrance into the circulation as emboli, and wherever they lodge they undergo division and give rise to new tumors.

Cysts of the liver are unusual. Are usually formed by the dilation of a bile-duct, but may be due to an obstruction of the lymphatics.

Echinococcus cysts are comparatively common. Are caused by the Tænia echinococcus, a parasite of the dog. The cysts may be either unilocular or multilocular; in the

latter case they may occupy the greater part of the organ. The wall of the cyst consists of an outer connective-tissue layer and an inner cellular layer from which secondary cysts may grow.

These cysts by their pressure cause atrophy of the liver substance, icterus, and ascites. They may rupture into the abdomen, neighboring organs, or at times into the vena cava with general distribution. If bacteria gain entrance, the cysts may become transformed into an abscess. Occasionally the contents of the cysts may be absorbed and replaced by cicatricial tissue.

Parasites.—The most common and important is the larva of the Tænia echinococcus, which gives rise to the cysts above described. *Amœba coli* in cases of tropical dysentery gains entrance and frequently gives rise to abscess formation. *Coccidium oviforme*, a common protozoa in lower animals, has been found in man. It forms growths that resemble somewhat adenomata. The *Distomum hepaticum*, *lanceolatum*, in the bile-ducts, and the *D. hematobium*, in the portal vein, are sometimes seen.

DISEASES OF THE GALL-BLADDER AND BILE-DUCTS

Angiocholitis or cholangitis, inflammation of the bile-ducts, is generally found in the common duct. It may, however, extend throughout the smaller ducts and capillaries. Is commonly secondary to inflammatory conditions in the stomach or duodenum. May be due to bacteria entering from the intestine or to irritation by the presence of a gall-stone. The catarrhal form is characterized by the presence of mucus, the purulent variety by the presence of pus.

The mucosa becomes reddened, swollen, edematous, and covered by mucus. If the inflammation becomes more severe, pus is secreted and perforation with abscess formation may occur. As a result of the swelling the outflow of bile is hindered and icterus follows. The duct above becomes dilated and frequently cystic; gall-stones may also form on account of the stasis.

If the swelling subsides bile begins to circulate and the

symptoms cease. If there has been permanent obstruction to the duct by connective-tissue formation, secondary changes within the liver take place, such as biliary cirrhosis.

Cholecystitis is an inflammation of the gall-bladder. It is commonly due to gall-stones within, but may be due to infection from without. When gall-stones are present the cystic duct is obstructed, the bile is unable to escape, and the gall-bladder becomes distended. The coloring-matter of the bile may eventually be absorbed and the bladder be filled with a colorless fluid. From the pressure of gall-stones ulcers may form and perforation into the peritoneal cavity, into the intestine, or through the abdominal wall occur.

When the inflammation is infectious, it may become purulent and the bladder be distended with pus, a condition called empyema of the gall-bladder.

The wall of the bladder is generally thickened and the mucosa ulcerated.

Stenosis of the bile-ducts is generally due to obstruction in acute inflammation by the thickening of the mucous membrane and the presence of mucus. In chronic inflammation there may be an overgrowth of connective tissue. Foreign bodies within or neoplasm from without may press upon the ducts and obstruct them. According to the location of the stenosis different conditions result. If the cystic duct be closed, the liver tissue is unaffected, but the bile is unable to escape from the gall-bladder, which becomes much distended. If the hepatic duct is obstructed, all the smaller ducts and capillaries above become dilated by the retained bile, and infection frequently occurs, giving rise to a suppurative cholangitis. Obstruction of the common duct will give rise to the dilatation of both gall-bladder and biliary ducts. As a result the liver becomes enlarged and deeply stained by bile-pigments. The cells in the outer zone of the acini contain pigment granules, and there is frequently an overgrowth of fibrous tissue along the ducts. Areas of necrosis may also be present.

Cholelithiasis.—Gall-stones, calculi of the gall-bladder, are solid masses resulting from the precipitation of various substances from the bile. They are most frequently found

late in life and most commonly in women. It would seem that they form about a nucleus composed of desquamated epithelium, bacteria, thickened mucus, or a foreign body from outside. Upon this body is deposited a layer of biliary salts; more layers are built up until a fairly large stone is found. This process is hastened if there is stasis and some decomposition of the bile. Instead of one large stone several may form, or there may be thousands, like grains of sand.

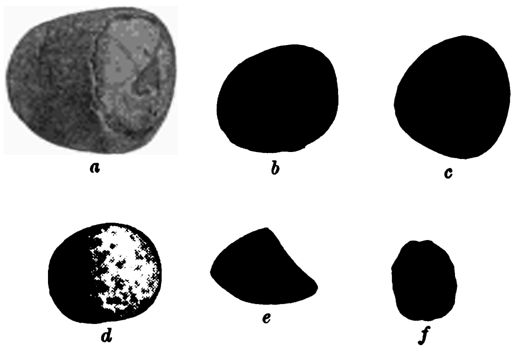

FIG. 144.—TYPES OF GALL-STONES. (From a photograph in the collection of Dr. Jepson, Sioux City, Ia.)

a caused complete intestinal obstruction for eight days; *b* and *c* were removed from the gall-bladder and show points of attrition; *d*, solitary stone removed from gall-bladder; no point of attrition; *e*, gall-stone of irregular shape, due to compression or moulding; *f*, solitary stone from common duct.

The shape depends upon the number present. If single, it may be round or ovoid. Usually the sides are flattened by mutual pressure, giving an irregular crystal-like form. The color of the stones varies, according to their composition, from light yellow, through various shades of brown to black.

They are generally formed in the gall-bladder, but may originate in the larger ducts.

The common variety is yellowish or brownish and is composed mainly of cholesterin and bilirubin in combination.

Other forms of calculi are made up of cholesterin, of bilirubin, and of calcuim carbonate.

Although biliary calculi may exist for years without giving rise to any disturbances, they frequently cause more or less serious lesions. The gall-bladder generally shows some catarrhal inflammation. The walls may exhibit slight or marked changes, they may be much thickened, ulcerated, or pouched. The calculi may escape from the gall-bladder as a result of ulceration with perforation. Is fairly common in cholelithiasis and most frequently perforate externally.

The most severe symptoms result when one of the calculi escapes from the gall-bladder into the cystic and common bile-ducts. This gives rise to biliary colic, a very severe form of pain which is associated with symptoms of collapse. If the stone is small, it can pass on through the ducts into the intestine. It may, however, become lodged in the lower part of the common duct, usually just above the outlet into the duodenal papilla. Following the blocking of the common duct there is retention of bile, which if long-continued gives rise to marked jaundice and lesions within the liver. The flow of bile may be resumed by dislodgment of the stone or by the establishment of a passage around the foreign body.

An accompanying symptom of biliary colic is an intermittent fever in which the temperature may go up to 104° or 105° F. at the onset. It then subsides and reoccurs.

Tumors of the gall-bladder are quite uncommon. About the only form is a primary carcinoma arising from the mucous glands. This growth seems to be quite frequently associated with gall-stones, which may be causative or merely the results of the stagnation of the bile. The liver is soon secondarily involved.

Jaundice or icterus is a staining of the tissues by biliary pigments that have been conveyed by the blood-stream. It is a symptom common to most diseases of the liver. There were formerly thought to be two forms of jaundice, the obstructive or hepatogenous and the non-obstructive or hematogenous. The latter variety probably does not really exist, all icterus being due to biliary coloring-matter. There

are, however, cases in which no mechanical obstruction can be observed, either by absence of bile in the feces or by lesions in the liver. This discoloration is seen in some infectious diseases and after experiments in which various substances have been injected into the blood.

Catarrhal jaundice resulting from obstruction to the duct by an inflammation of its mucous membrane is the commonest form. Any obstruction will, however, cause it. Microscopically it is seen that the biliary capillaries are distended and the liver cells contain more or less pigment. The bile escapes from its normal channels, is taken up by the lymphatics, from which it passes into the circulation and thence to the tissues throughout the body. The secretions and exudations of the body may be distinctly tinged. The tissue first stained is the intima of the blood-vessels; finally the skin and the sclera, where it is seen most characteristically. According to the duration, the color will vary from a light yellow to a dark bronze-green; the longer continued, the darker the color. If little or no bile escapes, the feces will usually be very light in color, clay-like.

The retention of bile within the body is generally accompanied by quite marked disturbances, particularly of the nervous system. As the flow of bile is re-established the discoloration gradually disappears.

PANCREAS

Malformations are unusual, except that the pancreas may frequently be composed of separated segments. Fragments of pancreatic tissue are sometimes found in the omentum, the walls of the intestine or of the stomach. Variations of the ducts are very common. The duct of Wirsung may be double, its relation to the duct of Santorini may vary greatly. Both ducts may open separately into the duodenum. Usually the duct of Wirsung and the common bile-duct open into the diverticulum of Vater.

Active hyperemia is present during digestion and as a stage in inflammation. *Passive hyperemia* occurs when there is some obstruction to the portal circulation. Is common

in alcoholics and may lead to the formation of connective tissue.

Acute hemorrhagic pancreatitis is an uncommon condition of unsettled origin. It occurs in men rather than in

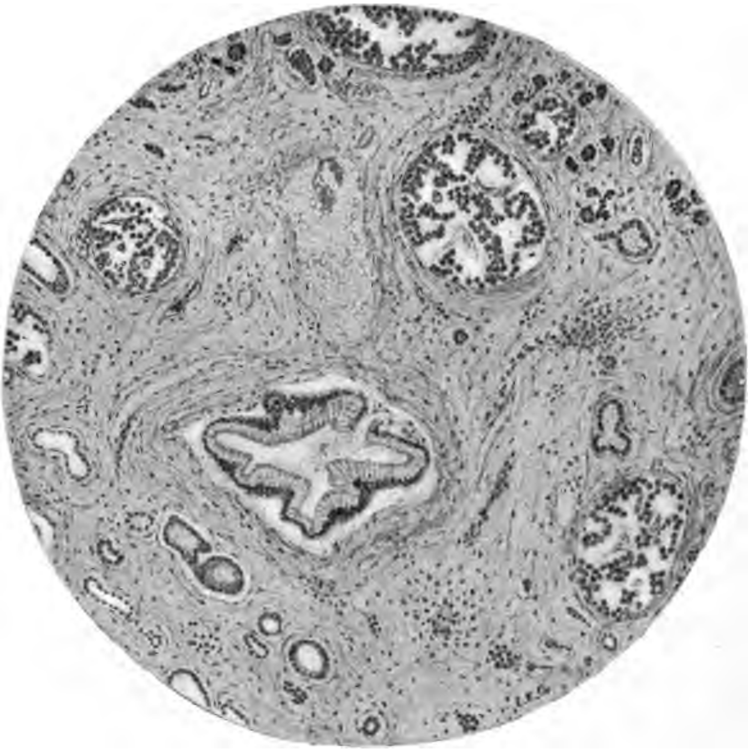

FIG. 145.—CHRONIC INTERSTITIAL PANCREATITIS FOLLOWING DUCT OBSTRUCTION, SHOWING ISLANDS OF LANGERHANS UNCHANGED THOUGH EMBEDDED IN SCLEROTIC TISSUE (Opie).

women and seems to be associated in many cases with cholelithiasis. By obstruction of the diverticulum of Vater bile may be forced up into the duct of the pancreas and give

rise to hemorrhagic pancreatitis. Various irritating substances when injected into the duct of Wirsung have given rise to a similar condition. The greater part of the pancreas is generally involved and death frequently comes on quite suddenly. Microscopically there is found extensive necrosis of the parenchyma and of the interstitial tissue as well. The stroma is the seat of a marked round-cell in-

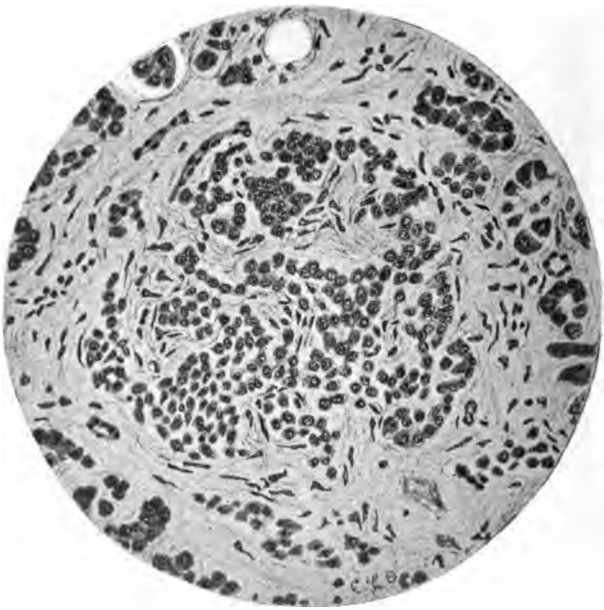

FIG. 146.—CHRONIC INTERSTITIAL PANCREATITIS OF INTERACINAR TYPE, SHOWING THE INVASION OF AN ISLAND OF LANGERHANS BY THE INFLAMMATORY PROCESS (Opie).

filtration and the fat frequently contains areas of necrosis. The epithelium is the seat of fatty degeneration and may be no longer recognizable.

Blood-vessels may be eroded and hemorrhage occur. Is impossible to sharply separate pancreatic hemorrhage and hemorrhagic pancreatitis.

Purulent pancreatitis may originate as such primarily or it may follow the hemorrhagic form. There may be a diffuse leukocytic infiltration or a formation of miliary foci of suppuration with here and there distinct abscesses. The infection may be due to the extension of inflammatory processes of a neighboring organ.

Gangrenous pancreatitis in many cases is a sequel of the acute hemorrhagic or it may follow the purulent variety. The gland is swollen, dark red, and soft; and may be converted into a dark, slate-colored, bad smelling mass. The entire gland may at last be changed into a large necrotic mass. Accompanying these changes numerous scattered foci of fat necrosis occur.

Chronic or interstitial pancreatitis is characterized by an overgrowth of fibrous tissue with more or less atrophy of the parenchyma. The connective tissue may be increased, either interlobular or interacinar. In the interlobular variety the islands of Langerhans are unchanged, while in the interacinar form the fibrous tissue surrounds and invades them. Cirrhosis is frequently found in alcoholics.

Syphilitic pancreatitis is not unusual in congenital cases. There is diffuse proliferation of fibrous tissue between the lobules and the acini. The cells also atrophy and disappear and the blood-vessels are the seat of a periarteritis. The islands of Langerhans are not affected. Gumma is rare, a few cases only having been reported.

Tuberculosis is infrequently met with, but may occur in the miliary form or, what is more rare, as a large caseous mass.

Atrophy of the pancreas is frequently found in old age, in local disturbances of the circulation, cachexia diabetes, and emaciation.

Hanseman's form of atrophy is consequent upon chronic inflammation. The organ is diminished in size and flattened, the fibrous tissue is usually adherent to adjacent organs, the epithelial elements are atrophic and are in part replaced by connective tissue. Hanseman thought that this form of atrophy was always present in cases of diabetes. Opie has found, however, that it is only in the interacinar form in

which there is a hyaline degeneration of the islands of Langerhans that diabetes occurs.

Fatty infiltration is not infrequently found accompanying various of the infectious fevers. The fat is deposited chiefly in the interlobular connective tissue and causes a secondary atrophy of the parenchymatous cells which may also contain some fat. The organ may be a trifle enlarged, soft, and grayish in color.

Fatty metamorphosis occurs as a result of severe infection, as in chronic phosphorous poisoning. The organ is soft and cloudy white.

Fat necrosis is a peculiar form of degeneration taking place in the fatty tissues of the pancreas and omentum. It appears as small, opaque, white areas in the immediate neighborhood of the pancreas or scattered throughout the organ itself. Several areas may become confluent and involve a large portion of the pancreas. The necrotic areas may be more widely disseminated, involving the omentum and the subperitoneal and the retroperitoneal tissue. They are opaque, whitish or yellowish, are sharply defined from the normal fat, and are generally surrounded by a narrow hemorrhagic zone.

Microscopically the affected tissues show absence of nuclei with presence of fat crystals and lime salts.

This form of necrosis is due to obstruction of the outflow of the secretion, or to the escape of the pancreatic juice into the peritoneal cavity. A fat-splitting ferment is present and it breaks up the fat into glycerin and a fatty acid. The acids are deposited as needle-like crystals with the broken-down cell. The glycerin is absorbed and the acids unite with calcium to form calcium salts, which give a gritty feel when the tissue is cut.

In the majority of cases fat necrosis is associated with either hemorrhagic or gangrenous pancreatitis.

Amyloid degeneration is found in cases of general amyloid disease, occurring either in spots or in streaks.

Hyaline degeneration is met with quite frequently. It involves the islands of Langerhans as well as the parenchy-

matous tissue. The affected portions stain with eosin and picric acid, but do not give the amyloid reaction.

This lesion is thought to have a distinct relation to diabetes mellitus. The islands of Langerhans are most numerous in the tail of the pancreas. In certain cases of diabetes there has been a marked absence of these bodies, due to hyaline change. The parenchymatous cells in such cases may or may not be involved. It would appear that as long as the islands remain unaffected diabetes will not be present, no matter how seriously involved the parenchyma is. These peculiar bodies of Langerhans apparently exert a distinct influence upon the metabolism of sugar.

As diabetes can be caused by lesions of the fourth ventricle it is evident that all cases cannot depend upon pancreatic lesions, but there is a distinct association in many cases.

Pigmentation may be due to hemorrhage, to atrophy, or old age. The epithelial cells contain brownish or yellowish granules that do not give an iron reaction.

Tumors.— *Sarcoma* is rare, but the round-cell and angiomatous forms have been described. They may occur as a part of a secondary sarcomatosis.

Carcinoma may occur primarily or after a similar growth in the stomach, duodenum, or gall-bladder. The primary form is found in the head of the gland and is most commonly scirrhus. It soon spreads and forms a large mass involving the greater part of the pancreas and the adjacent tissues. As it grows it may obstruct the bile-ducts, giving rise to icterus, or by pressure upon the duct of Wirsung set up a chronic interstitial pancreatitis sometimes accompanied by diabetes.

The growths generally originate from the cells of the acini and give an adenomatous structure to the tissue. They may arise from the cylindric epithelium of the ducts and form a scirrhous mass.

Obstruction of the pancreatic duct may cause it to become greatly dilated, so much so as to cause actual cyst formation. The contents are usually clear, but by infection may become purulent. Occasionally small cysts may be scattered through the organ.

Calculi in the duct are sometimes found. They may be a cause of obstruction.

DISEASES OF THE PERITONEUM

Malformations are occasionally met with. The omentum may be very small or unduly long. The mesentery may be very long, giving rise to enteroptosis. May allow hernias.

Circulatory Disturbances.—*Active hyperemia*, either localized or diffuse, is present during the early stage of inflammation, and is also met with in relation to tubercles and neoplasms. *Passive hyperemia* follows obstruction to the portal circulation. The veins may become much distended and tortuous and small hemorrhages into the subperitoneal tissue may be present.

Hemorrhage beneath the peritoneum in the form of petechiæ and irregular streaks is found in chronic passive congestion, in asphyxia, in phosphorous poisoning, and in some infections.

Hemorrhage into the peritoneal cavity results from rupture of a blood-vessel. When as a consequence of traumatism any of the internal viscera, as spleen or liver, rupture, blood will be present. Is also found in cases of rupture of abdominal aneurysms, and of extra-uterine pregnancy, and from typhoid or other perforations.

The blood collects in the dependent portion of the abdomen and may coagulate or remain fluid. If the patient recovers the blood may be absorbed without any permanent changes, although adhesions sometimes form.

Ascites or a collection of serous fluid within the peritoneal cavity is frequently seen. It may be due to obstruction of the portal circulation, especially in atrophic cirrhosis of the liver or as a part of a general dropsical condition in cardiac and renal disease.

It is also found in some local diseases of the peritoneum, as tuberculosis, etc.

The ascitic fluid is generally clear, straw-colored, with a small amount of albumin, which rarely coagulates spontaneously. The amount may vary from a few cubic centimeters to several liters and may become so great as to cause marked

inconvenience by distending the abdominal cavity and by pushing the diaphragm upward. This latter may cause extreme dyspnea. If the fluid is removed, it frequently collects again and again. If adhesions have formed, there may be localized collections of fluid.

If there has been obstruction to the thoracic duct, the ascitic fluid is frequently milky in character, due to the presence of chyle (*chylous ascites*). This fluid contains fat droplets as well as the red and white cells that are ordinarily present.

Sometimes there may be a collection of fluid between the layers of the omentum.

When the ascites has existed for a long time there is nearly always a secondary chronic inflammation of the peritoneum with thickening.

Peritonitis, inflammation of the peritoneum, may be primary or secondary. This serous membrane covers such a large surface and so readily absorbs fluids that infection may take place with comparative ease.

Primary or idiopathic acute peritonitis arises through the infecting agent being carried by the blood from a pyogenic focus in some distant part of the body.

Secondary acute peritonitis is the more common form. It follows local injury to the peritoneum, as a result of injury or disease, the infecting agent being carried generally by the lymphatics.

Peritonitis is brought about by infectious inflammations of neighboring tissues, particularly in septic conditions of the female genital organs, by perforations of the stomach or intestines, by appendicitis, by strangulation of the bowels, etc.

According to the extent of the lesion the peritonitis may be localized or general. The severity of the disease also differs greatly.

The membrane at the point of infection is at first hyperemic, is dull, and a serous or serofibrinous exudation soon appears. This rapidly becomes purulent or may have been so from the beginning. If the process has not been a very rapid one the affected area will be covered by a thick whitish or creamy

layer of fibrin. As the exudate increases in quantity it collects in localized pockets among the coils of intestine. The fibrin may undergo organization, adhesions form, and the purulent matter be surrounded and walled off. It may be absorbed, infiltrated with lime salts, or replaced by fibrous tissue. The pus may burrow and empty either externally or into some hollow organ. If the adhesions have not been sufficiently dense, the abscess may break through and infect the greater part of the peritoneum. In such a severe form the serous membrane becomes infiltrated and partially disorganized.

Localized peritonitis is not usually fatal, but in the general form recovery is rare. When peritonitis subsides and the individual lives, adhesions of varying extent remain. These eventually become transformed into dense fibrous bands that may cause very severe trouble by binding the coils of intestine together or by so compressing them that the bowel becomes more or less obstructed.

As a result of the acute inflammation the peristaltic action of the intestines is at first stopped by spasmodic contractions. In a very short time the muscle fibers become paralyzed and there is then almost complete cessation of motion. General septicemia may follow the peritonitis.

In the new-born peritonitis generally follows septic infection of the umbilical cord.

Chronic peritonitis may follow in the course of acute peritonitis, particularly if it were localized. When encapsulated collections of pus have failed to be absorbed the peritoneum adjacent shows marked chronic thickening. Local thickenings may also be due to chronic disease of the underlying organ. This is particularly the case at times on the liver and spleen. The membrane becomes very thick, white and smooth, and resembles icing of a cake, the so-called "Zuckerguss" organs. Chronic peritonitis is particularly common in the neighborhood of the female genitalia; all of which, uterus, tubes, and ovaries, may be united by dense bands of connective tissue. Is also always present in tuberculosis of the peritoneum.

Tuberculosis of the peritoneum is seldom primary, but is commonly found as a secondary lesion in similar disease of the intestine or mesenteric lymph-nodes. The condition may be local, being limited to the peritoneal surface of the intestine overlying tubercular ulcers; or it may be widely disseminated as a general miliary involvement. The lesions may coalesce and form large caseous areas or there may be extensive connective-tissue formation with adhesions causing the intestines to be bound together in one dense mass. Occasionally there may be considerable serous exudate present; if the exudate is purulent it generally indicates that there has been a secondary infection by pus-producing organisms. The exudate may at times be completely absorbed or remain as sacculated collections. The tubercles may heal by granulation and cicatrization and the individual get well.

The mesenteric lymph-nodes are generally enlarged and caseous.

Tumors.—Primary tumors are unusual, new growths being generally metastatic or the result of direct extension. *Fibroma* and *lipoma* are sometimes seen. *Sarcoma* is rare. *Endotheliomata* are quite frequently found. As a rule, there is not a localized growth, but is distributed throughout the peritoneum, giving somewhat the appearance of tuberculosis. The omentum is probably the seat of the primary growth.

Carcinoma is nearly always secondary, but it is thought that primary carcinoma might arise from fragments of epithelial tissues, from fetal remnants, or from portions of intestine pinched off in fetal life. There is usually a general distribution of tumor nodes of all sizes over the greater part of the peritoneum. When the nodules are widely distributed the condition is known as "*carcinomatosis*." There is always some inflammatory reaction, so adhesions are quite common. The carcinoma may extend from various abdominal organs, as the uterus, tubes and ovaries, and intestines. A gelatinous or colloid cancer of the stomach or intestine is usually soon followed by a similar growth involving the peritoneum. Such a tumor contains large and small masses

of clear colloid material resulting from degeneration of the cells.

Cysts are sometimes encountered, the usual form being due to a dilatation of lymph-vessels.

Parasites are rare, but echinococcus cysts have been found as well as filaria and actinomyces.

CHAPTER XXII

DISEASES OF THE URINARY ORGANS

THE KIDNEYS

Malformations.—Rarely both kidneys may be absent, but the fetus is incapable of living. Absence of one kidney is more common and is not incompatible with life. The left organ is usually wanting and the right undergoes compensatory hypertrophy so as to perform its extra work.

Atrophy of a kidney is not infrequent, it being represented by a small body composed of connective tissue with very little glandular structure. A third kidney has been seen in a few cases. The *lobulation* of the kidneys during fetal life usually disappears by the tenth year, but it may persist till late life.

Horseshoe kidney is the result of the fusion of the two kidneys at either their upper or lower ends. The band of union may be purely fibrous or of renal tissue. The ureters, from two to four, arise from an anterior pelvis. The vessels are usually more numerous than normal and are generally anomalous.

One of the kidneys, usually the right, may become much displaced downward and hang from a much stretched peritoneal covering. Is the "floating kidney" and can give rise to many symptoms. The left may be displaced congenitally. The relaxation of the support of the right kidney may be due to disease or displacement of the liver, to tight lacing, or to a dragging exerted by the stomach or transverse colon. The perineal fat decreases, the peritoneal covering stretches, and the kidney is easily moved. The nerves and vessels and the ureters are put in a state of tension and severe symptoms arise. If the pedicle becomes twisted the circula-

tion may suffer and by obstruction to the ureter urine collect and give rise to a hydronephrosis.

Circulatory Disturbances.—*Anemia* of the kidneys is present in general anemia; or it may be due to gradual obstruction of the arteries, either by disease or by pressure from without. If the obstruction has been sudden, necrosis is usually present. The organ is small and light in color. If the anemia continues, there is interference with the secretion of urine and atrophy may ensue. Fatty degeneration appears first in the glomeruli but soon involves the parenchyma.

Acute hyperemia is generally a stage of acute inflammation in infectious conditions. Numerous irritating bodies that are excreted through the kidneys may give rise to the hyperemia. Such are certain poisons, as cantharides, carbolic acid, toxins of infectious conditions, as scarlet fever, those present in cases of extensive superficial burns. The kidneys are slightly enlarged, dark red in color, and soft. The capsule strips easily and on section much blood escapes. In the cortex are seen numerous minute red spots, the Malpighian bodies, and the congestion exists throughout. The epithelium usually shows some cloudy swelling. The urine may contain a few erythrocytes, a trace of albumin, and cylindroids.

Passive hyperemia may be due to cardiac or pulmonary disease, to thrombosis of the inferior vena cava or of the renal veins, or to pressure upon these veins from without. Sometimes there may be an acute passive stasis, the organ becomes much distended and death may result. Ordinarily the kidney is enlarged, dark in color, and soft, with a capsule that strips readily. The stellate veins are prominent, blood drips from the cut surface, the Malpighian bodies are enlarged and the bases of the pyramids are markedly congested. If the hyperemia is of long standing there is always more or less hyperplasia of the connective tissue. So much so that the organ, although enlarged, may be hard and dark in color, owing to the deposition of pigment; is known as *cyanotic induration*. The capsule is usually somewhat adherent and the surface of the organ irregular. The epithelial cells show some fatty degeneration and atrophy.

The amount of urine is diminished and contains varying numbers of red and white blood-corpuscles, some albumin, and a few hyaline or granular tube casts.

Hemorrhage in the form of punctate collections may occur in severe acute or passive hyperemia. The blood will be found within the interstitial tissues, in the tubules, or in Bowman's capsule; it may escape by actual rupture or by diapedesis. Large hemorrhages usually occur only as a result of trauma, but may be due to infarction. The urine will contain blood either as free corpuscles or as the so-called blood-cast.

Arteriosclerosis.—The kidney may show most marked sclerotic changes, such as are found elsewhere in the body. All the vessels are not uniformly involved, so there are irregular appearances. The vessels become gradually occluded by a thickening of the walls with a decrease in the lumen. The areas supplied by such vessels undergo atrophy, degeneration, and frequently become infiltrated with lime salts. Fibrous connective tissue forms to some extent, and as this contracts it compresses the urinary tubules. Excretion continues, the tubules dilate, and small retention cysts form both on the surface and in the kidney tissue. The kidney is smaller than normal, firm, and its surface shows depressed areas representing the atrophic portions, at which points the capsule may strip with difficulty.

Microscopically the alterations in the blood-vessels are seen and the glomeruli in many instances are surrounded by greatly thickened capsules which may contract until the capillary tufts have been reduced to small fibrous masses. If there is much connective tissue present it indicates that there has been a chronic inflammation of the organ, an interstitial nephritis. This is not uncommon, as the same etiologic factors will bring about both the arteriosclerotic and the interstitial changes. Is caused by syphilis, chronic lead poisoning, gout, and old age.

In this form the urine is practically unchanged.

Infarcts of the kidney are common, as the arteries have practically no anastomoses with each other. In the *anemic*

infarct the appearance varies according to the age of the lesion. When recent, there is a pale, circumscribed elevation on the surface of the kidney, surrounded by a narrow zone of hemorrhage. If old and connective-tissue formation has occurred, there is a depressed area. On section it is seen that the involved portion is conical in shape with the apex directed toward the hilum. The epithelium becomes cloudy and soon degenerates. This area becomes transformed into scar tissue in the course of time. In *hemorrhagic* infarcts the process is the same except that the area has become filled with blood which gives it its dark appearance.

Thrombosis of the larger renal veins may give rise to congestion and edema with degeneration and necrosis of the area involved.

Embolism is not uncommon, and on account of the lack of anastomoses of the renal arteries usually results in infarction. Embolism may be single or multiple, and if bacteria are present suppurative processes are present in addition to the already mentioned lesions.

Degenerations.—*Parenchymatous degeneration* or *cloudy swelling* is a condition in which the secreting epithelium is involved. It occurs in diphtheria, scarlet fever, and in most of the infectious diseases.

If the conditions that bring about this change persist, the cloudy swelling is very apt to pass over into the acute parenchymatous nephritis. In cloudy swelling the kidney is larger than normal, somewhat softer, and yellowish or pale gray. The cut surface shows the Malpighian bodies as small red dots and the pyramids are often markedly congested. The cells in the tubules are swollen and cloudy on account of the presence of numerous minute granules, and the nuclei are hidden. The kidney may return to the normal or else acute Bright's disease or fatty degeneration may ensue.

Fatty degeneration may follow cloudy swelling or arise as a consequence of various diseases, as pernicious anemia or tuberculosis. As fat is never normally present in renal epithelium, its occurrence is always pathologic and is in-

dicative of a degenerative process. It is due to the lack of nutrition, and at times is added a toxic effect of some substance in the circulating blood.

The kidney is about the normal size or smaller, is soft, the cortex is not thinned, and the organ is uniformly yellowish unless there is much congestion present. The fat may be diffusely present, or, what is quite common, occur in

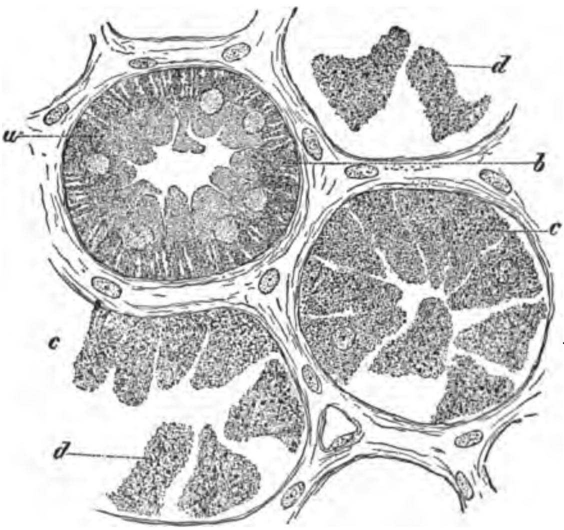

FIG. 147.—CLOUDY SWELLING OF THE KIDNEY EPITHELIUM. × 800 (Ziegler).

a, Normal epithelium; *b*, beginning cloudy swelling; *c*, marked degeneration; *d*, desquamated degenerated epithelium.

streaks along the collecting tubules of the pyramids. It is also seen as minute yellow points. The cells contain granules or oil drops of varying size.

Amyloid degeneration of the kidney follows the same causes as bring it about in the liver and spleen, such as the long-continued suppuration in bone diseases, in tuberculosis, and in syphilis. The kidney is usually much enlarged,

harder than normal, and grayish or slightly yellowish in color. If the process is not general the organ will appear mottled, areas of fatty degeneration being present. This degeneration begins, as a rule, in the capillaries of the glomeruli, from which it extends to the neighboring connective tissue, but not at the epithelium. If the degeneration has not been extensive fatty changes are uncommon, as the blood-supply may still be sufficient for the nutrition of the epithelium. Microscopically the glomeruli are seen to consist of a homogeneous and translucent mass in which the capillaries cannot be distinguished. The capsule of Bowman may also be involved. As the circulation is interfered with the organ becomes anemic, and fatty degeneration of the epithelium occurs. The amyloid areas give a mahogany brown color on the addition of Lugol's iodin solution. The urine is diminished and contains albumin and hyaline casts occasionally.

Glycogen is found in the epithelium in the loops of Henle in cases of diabetes. The cells, instead of being granular, are homogeneous and give the dark brown color with iodin if the tissue has not been put in watery fluids. Glycogen differs from amyloid in being soluble in water.

Calcification may take place in old degenerated areas in the connective tissue or in the necrotic epithelial cells. Under this heading come the so-called "calcareous infarcts," in which various salts are deposited, particularly in the straight collecting tubules. They may be composed of urates, and the presence of such infarcts has been thought to indicate that a new-born child has breathed.

Nephritis, inflammation of the kidney, or Bright's disease is brought about by many conditions, all of which in some way produce an irritation of the kidney by means of the circulation. It follows in the course of poisoning by certain chemicals, such as arsenic, mercury, phosphorus, cantharides, and turpentine; especially in the course of the acute infectious diseases, and also in certain chronic infections, as syphilis and tuberculosis. Nephritis may be acute or chronic and *parenchymatous* or *interstitial*, according to whether the changes in the epithelium or in the connective tissue pre-

dominate. If both are more or less equally involved the term *diffuse* is applied.

Acute parenchymatous nephritis is found in the course of the acute infectious fevers, particularly in diphtheria, scarlet fever, and smallpox. The kidneys are usually enlarged, red in color, soft, and edematous. The capsule strips

FIG. 148.—ACUTE PARENCHYMATOUS NEPHRITIS (CATARRHAL) (McFarland).

a Tubule denuded of a large part of its epithelium; *b*, cells in a condition of degeneration; *c*, mass of desquamated cells in a tubule.

easily. On section bloody fluid escapes. The cortex is thicker than normal and is much paler than the medulla, which is dark red. The anemia of the cortex is due to the swelling of the cells which compress the capillaries. The

epithelium is swollen, cloudy, and in many places has become desquamated. This is most marked in the convoluted tubules.

In some cases, particularly in scarlet fever, the changes may be most noticeable in the glomeruli, the *glomerulo-*

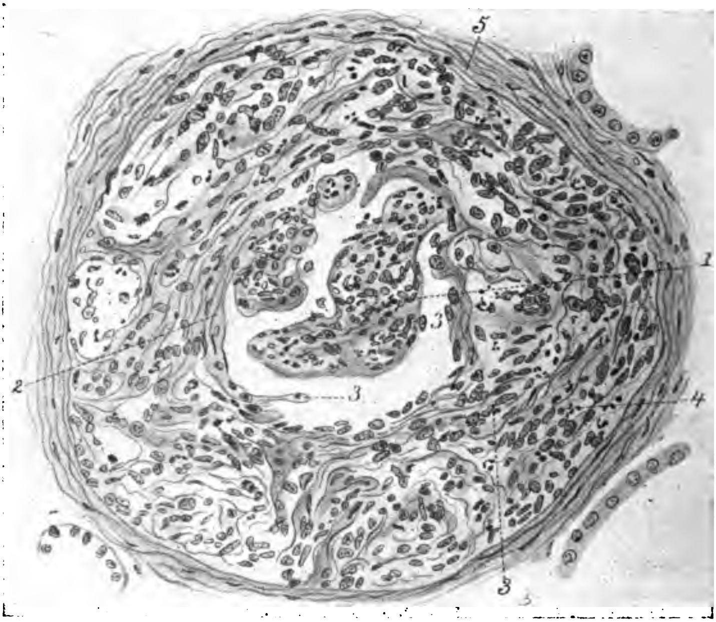

FIG. 149.—CHRONIC GLOMERULONEPHRITIS. × 320 (Dürck).

The capsule fibrillated and thick (5); septa extend inward between the desquamated epithelial cells (3) and leukocytes (4); 2, innermost layer of connective tissue surrounding the greatly diminished tuft (1), which is covered with epithelial cells, the lumen containing leukocytes.

nephritis. In this variety the capsular space contains desquamated epithelium from the capsule, red and white blood-cells, granular matter, and an albuminous exudate. The cells may show fatty degeneration. The erythrocytes may be sufficiently numerous to form blood-casts.

The glomeruli are seldom alone involved, the more common condition being a combination with changes within the tubules.

Ordinarily either of the two preceding varieties terminate in the *acute diffuse nephritis*, a form in which there are exudative or proliferative changes in the interstitial stroma.

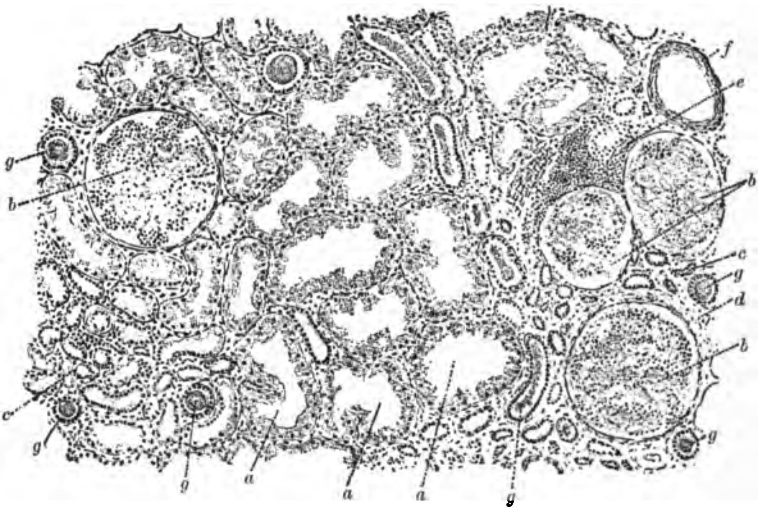

FIG. 150.—CHRONIC PARENCHYMATOUS NEPHRITIS (Kaufmann).
a, Convoluted tubules with cloudy swelling of the epithelium; *b*, glomeruli, more or less degenerated; *c*, atrophic tubules; *d*, sclerotic interstitial tissue; *e*, round-cell infiltration; *f*, blood-vessel; *g*, tube-casts in tubules.

The kidney is larger than normal and may be either dark and congested or pale on account of parenchymatous changes. The cortex is much increased in thickness and shows areas of congestion. The capsule strips easily. The microscopic changes are many. The epithelial cells may be cloudy or swollen, show fatty degeneration, or at times be necrotic. Accompanying these changes there may be a well-marked

round-cell infiltration in the connective tissue. There may also be small areas of hemorrhage into the tubules or the capsule of Bowman.

The urine is decreased in amount and at times suppressed, has a high specific gravity, is dark in color and contains many casts. Microscopically are seen red and white blood-cells, desquamated epithelium, and tube casts, particularly the epithelial and granular forms.

Chronic parenchymatous nephritis may be the result of numerous attacks of acute nephritis, or it may have pursued a chronic course from the outset. It is probably due to the persistent presence in the circulation of some irritating toxic substance. It is characterized by chronic degeneration of the secreting epithelium and by a proliferation of the fibrous connective tissue.

The usual variety is the *large white kidney*. The kidney is much increased in size, is smooth, pale, and softer than normal. The capsule strips easily. The exposed surface presents a somewhat mottled appearance. On section the cortex is seen to be much thickened and paler than the pyramids, which are usually congested and reddish. The cortex may show scattered punctate hemorrhages.

If the nephritis has existed for a long time, the kidney may become smaller on account of the contraction of the new-formed connective tissue. The organ is then smaller than normal, pale, and granular, the *pale granular kidney*. The epithelium becomes markedly degenerated and the connective tissue contracts and compresses the parenchyma. The capsule is adherent and cannot be removed without bringing away portions of the kidney.

Microscopically the chief change present is a fatty degeneration of the epithelium in the tubules and the glomeruli. The tubules may be filled with granules from the broken-down cells, and erythrocytes may be present. Round-cell infiltration of varying degrees will be found in the interstitial tissues. The Malpighian bodies generally show a proliferation of their epithelium, the capsule of Bowman may become much thickened, and the walls of the capillaries also

increase in thickness. The amount of connective tissue is never as great as in the chronic interstitial form.

The urine will contain granular and hyaline casts and varying amounts of albumin.

Acute interstitial nephritis or *suppurative nephritis* is the result usually of hematogenic infection by micro-organisms, or it may be due to extension of an inflammation of the pelvis of the kidney or of a neighboring tissue. The organisms gain entrance to the kidney as emboli and usually become lodged in the capillaries of the glomeruli. There is an extravasation of round-cells and leukocytes into the capsular space and minute foci of suppuration are formed. The irritating products soon cause destruction, with necrosis of the adjacent cells. There is generally some extravasation of blood surrounding the areas of suppuration. The process may terminate by the absorption of the exudate with connective-tissue formation. If the lesion becomes more extensive distinct abscesses may form which may discharge into the tubules or be absorbed and cicatrized.

If the infection has followed a suppurative pyelitis the kidney will be found on section to contain light yellowish colored streaks in the pyramids and medulla. These are composed of tubules that have become filled with pus. Sometimes several of these foci may coalesce and form a larger abscess, which may discharge its contents into the pelvis of the kidney or upon the surface of the kidney; or it may become absorbed and undergo cicatrization. The suppurative process may go on to such a point that the entire kidney becomes converted into a sac filled with pus.

Chronic interstitial nephritis is a form of kidney inflammation characterized by a continual increase in the amount of interstitial connective tissue associated with an atrophy of the secreting cells. It is found in alcoholism, syphilis, chronic lead poisoning, and is frequently associated with general arteriosclerosis.

The kidney is small, dark red in color, firm, and granular, the *red granular kidney*. The irregularities are due to the contraction of the connective tissue. The capsule strips

with great difficulty, tearing away portions of the renal substance with it. On the surface are seen small cysts filled with clear fluid. These are due to the obstruction of a tubule by the pressure of the connective tissue. The

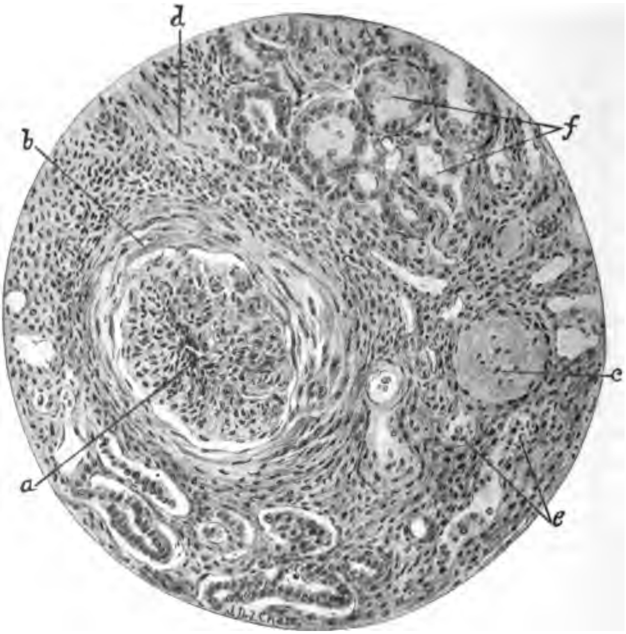

FIG. 151.—CHRONIC INTERSTITIAL NEPHRITIS (McFarland).

a, Still functional glomerule with (*b*) mass of newly formed connective tissue surrounding Bowman's capsule; *c*, totally destroyed glomerule; *d*, newly formed cellular connective tissue; *e*, atrophic uriniferous tubules; *f*, slightly altered uriniferous tubules.

tissue cuts with great difficulty, being almost cartilaginous at times, and presents a typical appearance. The cortex is generally very thin with some places of almost normal thickness. Over the thin areas the capsule is usually considerably thickened. The medulla shows little change.

Microscopically the picture is very definite, although all portions of the kidney may not be equally involved. As the glomeruli are the parts first brought into contact with the circulating toxic substances, it is there, as a rule, that the processes begin. The glomerulus becomes slowly transformed into a more or less homogeneous body that loses all lobulations. At the same time the capsule becomes greatly thickened and the glomerulus is finally transformed into a minute fibrous nodule. The intertubular connective tissue increases until eventually the tubules may become completely atrophic, through compression. Although many of the tubules are atrophic, others will be found markedly dilated, so much so that small cysts may form. There is also a thickening of the walls of the blood-vessels. All these processes may go on to a point where there is very little renal secretory structure left. The parenchyma also shows some changes, but not so markedly as in the chronic parenchymatous variety. There is some atrophy and fatty degeneration.

The urine is generally increased in quantity, of a low specific gravity, with little or no albumin. A few casts of the hyaline and waxy character are found.

Tube casts are peculiar bodies that are formed within the urinary tubules and that are composed of various albuminoid substances, some of which react like fibrin. *Hyaline casts* are pale, almost transparent, structures reacting like fibrin. They may vary greatly in length and also in thickness; are found most commonly in acute parenchymatous nephritis, but are also present in the chronic parenchymatous and interstitial varieties. The hyaline cast is the foundation of many of the other forms. Its surface is adhesive, and according to the substances upon it, we have *granular*, *epithelial*, *leukocytic*, and *blood* casts. Some blood casts may, however, be formed by the coagulation of extravasated blood within a tubule. *Granular* casts may be dark or pale according to the amount and form of the material composing them. Are found usually in chronic nephritis. The *waxy* cast is a rather large, translucent, and solid appearing body that is found especially in chronic interstitial nephritis and in amy-

loid diseases. At times it may give an amyloid reaction with iodin.

The effects of nephritis are particularly noticeable in the cardiovascular system when the renal disease is of a subacute or chronic type. There is a hypertrophy of the heart, especially of the left ventricle, which may become greatly enlarged. The reason for this hypertrophy is not clearly understood. As the kidneys normally secrete urea, chlorids, phosphates, uric acid, urates, and oxalic acid, the accompanying changes may be due to the retention of these substances within the circulation. As in chronic renal disease there is always more or less arteriosclerosis present, the cardiac enlargement may be due to the extra amount of work required to force the blood through the thickened and less elastic vessels.

The serous membranes in acute nephritis may show inflammatory changes, such as acute endocarditis, acute pericarditis, and pleuritis. *Edema* is particularly common in acute parenchymatous nephritis, especially if the glomeruli and vessels are involved. The edema appears first in the eyelids and hands, but as the disease progresses and the blood-vessels degenerate it spreads over the entire body. Death may result from edema of the lungs. Uremia is also a frequent condition, due probably, to the retention within the circulation of various toxic substances.

Tuberculosis of the kidney may be due to primary hematogenic infection or to secondary involvement following similar disease of other portions of the genito-urinary tract. It may be a part of a general miliary tuberculosis and present numerous minute grayish white tubercles scattered throughout the renal substance, particularly in the cortex. The foci may be surrounded by a narrow zone of congestion.

When there has been an ascending infection from the ureters or a primary local tuberculosis the changes are quite characteristic. The process may begin as a miliary tubercle, which by invasion and lymphatic extension spreads through the organ. The apices of the pyramids are involved and the disease extends through them to the cortex. These areas

undergo coagulation necrosis, soften, and eventually discharge their contents into the pelvis of the kidneys, leaving an irregular cavity. On section there are seen numerous large cavities communicating with the pelvis of the kidney. The discharged material infects the mucous covering of the pelvis and the disease gradually extends downward along the ureter until the entire urinary tract may be involved. This, of course, when the tuberculosis has been primary in character and not due to an ascending infection. The ureter may become obstructed, and the kidney undergo dilatation, thus forming a cold abscess of the kidney, the organ being changed into a sac with thick walls and containing tubercular pus.

FIG. 152.—TUBERCULOUS PYELONEPHRITIS (modified from Bollinger).

Syphilis is infrequent and not definite in its manifestations. There have been found gumma giving rise to thick stellate scars.

Tumors of the Kidney.—*Fibromata* in the form of small nodules are occasionally found. *Lipomata* and *leiomyomata* are sometimes encountered.

Sarcoma is quite common and is either congenital or else

appears, as a rule, very early in life. The tumor may attain considerable size, is usually grayish in color, although it may be red if very vascular, and may be quite soft. Generally the growth is composed of round or spindle cells, but not infrequently are found fibers of striped muscle, the so-called *rhabdosarcoma*. Sarcoma may occasionally be found in later life. Such a tumor differs from the congenital form in being slow in growth and not giving metastases till late. The congenital form is rapidly malignant and destructive.

FIG. 153.—CONGENITAL CYSTIC KIDNEY (Specimen 2816, Museum N. Y. Hosp.).

Of the epithelial tumors the *hypernephroma* is the most common. It is derived from portions of adrenal tissue that have been included within the kidney during its development. The structure of the tumor resembles that of the adrenal gland, except that the cortical elements are the more prominent. The neoplasm may be small and remain circumscribed or it may take on a rapid growth and become destructive. The cells contain fat and glycogen.

Adenoma is rare. It occurs as small circumscribed nodules composed of glandular alveoli, which may show papillary outgrowths and also at times be cystic.

Carcinoma as a primary growth is unusual and secondary

metastases are not common. The secondary form makes its appearance as small scattered nodules. The carcinoma may become quite large, and destroy the renal tissue, and is frequently associated with hemorrhages into the tissue.

Cysts of the kidney are quite common and are of various forms. They may be single or multiple, large or small. In the majority of cases they appear as numerous small collections of fluid scattered over the surface of the kidney. They are simple retention cysts due to the obstruction of the tubule below the glomerulus; are especially common in chronic interstitial nephritis. Occasionally a kidney may contain a single large cyst and otherwise be apparently normal. Is probably due to the obstruction of a tubule.

The kidneys may be congenitally cystic, and in such a case present a characteristic appearance. Both kidneys are generally affected and are filled with numerous cysts, some of which may be as large as a walnut. These may be filled with a urinous or even a colloid material, and are separated from each other by a very thin stroma of connective tissue. The organs may be very much enlarged. Generally such a condition is incompatible with life, but similar lesions may be found in adults. As long as the remaining renal substance is able to maintain the excretion the individual will live, but when the organs become incompetent death may ensue from uremia.

Hydronephrosis is a cystic dilatation of the kidney resulting from an obstruction of the ureter. When the ureter is obstructed, as by a calculus, by inflammatory changes, by twists or kinks, or by pressure from new growths either within or similar conditions on the outside, it and the pelvis of the kidney will begin to dilate. The urine, being unable to escape, collects and gradually causes the tissues to stretch. The pelvis becomes larger, the calices are flattened out, and the renal tissue becomes atrophic until, as a result of the combined pressure and atrophy, there is a mere shell of kidney substance remaining. The fluid contained within the sac is at first practically normal urine. As long as there is any secretory tissue left urine is excreted, but when that ceases the salts in the fluid are either precipitated or absorbed and

the remaining liquid is watery. Such cysts may become infected or hemorrhages may take place within them. When filled with pus, the condition is known as *pyonephrosis*.

Nephrolithiasis.—*Renal calculi* are quite frequently found in the pelvis of the kidney and are composed of material precipitated from the urine. They may occur in the form of fine particles like sand or they may be so large as to be unable to pass out through the center. When small, the calculi can pass from the kidney without giving any pain. As they become larger they may pass out and give rise to severe renal colic; if quite large, the ureter may be completely blocked, and dilatation and atrophy follow. The concretions may also vary in shape, some being round and smooth, while others may be very rough, and if large send prolongations into the calices. The commonest variety is composed of uric acid and oxalate of lime, but phosphatic stones are found occasionally. The color varies according to whether uric acid and urates or the phosphates predominate.

The presence of calculi may cause degeneration and atrophy as a result of pressure, and suppuration is quite common. Obstruction of the ureter gives rise to varying degrees of hydronephrosis.

The presence of calculi seems occasionally to antedate the formation of a carcinoma.

DISEASES OF THE URETER

There may be obstructions due to congenital atresia or to various diseases and neoplasms. The result of such a condition is a dilatation of the ureter above the obstruction and of the kidney (hydronephrosis).

Pyelitis, or inflammation of the pelvis of the kidney, is met with in the course of various infectious diseases, as typhoid fever, scarlet fever, smallpox. In such cases is seldom of any severity. The most important causes are local infection and calculi. Infection may take place through the presence of pyogenic organisms within the urinary apparatus, and according to the degree of severity the inflammation may be catarrhal, hemorrhagic, suppurative, pseudo-

membranous, or ulcerative. In the suppurative form there is nearly always an involvement of the renal tissue, a *pyelonephritis*. If the ulcerated form is severe, perforation may take place and the purulent contents escape into the surrounding tissue, giving rise to a *perinephritic* abscess, the pus collecting in the areolar and fatty tissue about the kidney. It may remain encapsulated, and compress the kidney, or it may

FIG. 154.—TUBERCULOUS NODULE IN THE WALL OF THE URETER, WITH BEGINNING HYDRONEPHROSIS (from a specimen in the Museum of the Philadelphia Hospital, Phila.).

burrow through the deeper tissues and discharge below Poupart's ligament.

In chronic pyelitis the mucous membrane may become much thickened, contain ulcerations, and be covered in places by a precipitation of the salts from the urine. The kidney in this form is often the seat of chronic inflammation, suppuration, or atrophy.

If the ureter becomes obstructed, the pelvis of the kidney may be filled with pus, a *pyonephrosis*.

Calculi may lodge within the ureter and give rise to varying disturbances, from acute renal colic to obstruction with subsequent hydronephrosis. Hemorrhage may be caused by laceration of the mucous membrane and suppuration is not uncommon.

Parasites at times find their way into the ureters and pass up to the kidney. A ureter may also become the seat of tubercular changes.

DISEASES OF THE BLADDER

Malformations of the bladder are quite common. The most usual form is a lack of union along the anterior median line with failure of closure of the abdominal wall, *exstrophy* of the bladder. Is usually associated with epispadias, or with division of the clitoris. Occasionally there may be a communication with the rectum or the vagina. Sometimes there is no urethra.

The urachus may remain patulous and urine be discharged at the umbilicus or may be retained in the anterior abdominal wall as a cyst. Diverticula may occur, usually in the anterior wall. The bladder may be completely lacking, the ureters emptying directly into the urethra, or the organ may be divided into two portions by a septum.

Hypertrophy of the bladder may follow any chronic interference to the outflow of urine. The muscular coat of the wall becomes much thickened and the mucous membrane also increases in thickness and is thrown into folds. Indications of chronic inflammation are also usually present.

Dilatation of the bladder may be congenital or acquired. It is due either to obstruction to the escape of urine or to paralysis of the muscular coat of the wall. As a rule, the condition results from long-continued interference with the escape of urine, and is accompanied by a hypertrophy of the walls with thickening of the mucosa. The fibrous bands are prominent and the mucosa in between is pouched. Diverticula are quite frequent. If the dilatation has taken place suddenly, as in paralysis, the vesical walls are very thin. Such a weakening is often accompanied by rupture, with peritonitis.

The bladder may occupy an abdominal position, particularly in women, when there has been some laceration of the perineum. Its walls may prolapse into the vagina, forming a cystocele. At times it may be completely inverted.

Rupture of the bladder may follow severe injury or acute dilatation. The rupture generally occurs at the base and is followed by peritonitis and death. As a result of traumatism the injury commonly occurs near the neck of the bladder and is followed by extravasation of urine into the surrounding tissue, which generally gives rise to a severe phlegmonous cellulitis.

Fistulous communications with the vagina or rectum are not uncommon in women as a result of injuries received during childbirth.

Circulatory Disturbances.—*Active hyperemia* is usually dependent upon infection by some micro-organism or due to the presence in the urine of irritating substances. The mucous membrane is diffusely red.

Passive hyperemia is due to thrombosis of or pressure upon the inferior vena cava. The mucous membrane is dark red in color, the vesical veins at the neck of the bladder become distended and varicose, and there is some catarrhal inflammation. Severe hemorrhage may occur from a rupture of one of the varicose veins or the veins may be the seat of thrombosis.

Hemorrhage may be caused by injuries, calculi, malignant disease or result from ruptured varicose veins.

Inflammation.—*Acute cystitis*, inflammation of the bladder, may be due to the presence of pus-producing organisms that have gained entrance from the urethra or to the presence of irritating substances within the urine. The infecting agent may have been introduced by the use of unclean instruments in catheterization. The bladder is usually empty or else contains a small amount of cloudy urine that throws down a sediment composed of desquamated epithelium, mucus, pus cells, and bacteria. The mucosa is hyperemic, swollen, and edematous. The process may subside in a short time or it may become *pseudo-membranous*. The inflammation extends into the deeper tissues, necrosis of the

epithelium with ulceration takes place, and over these areas is formed a pseudo-membrane. The greater part of the vesical walls may be thus covered.

Phlegmonous cystitis may be a further stage of the above processes, but it usually results from a rupture of the bladder. The vesical walls and the surrounding tissues become infected and are the seat of abscess formation.

Chronic cystitis may follow acute inflammation, but is generally caused by some chronic obstruction to the escape of urine. As a result of obstruction there is a retention of urine with subsequent infection. Decomposition follows and the irritating products set up a chronic inflammation. The mucous membrane becomes much thickened and even polypoid, is reddened, and frequently ulcerated. Lime salts may be deposited in the degenerated tissues. The muscular fibers hypertrophy, but they gradually lose their strength and the urine is not discharged. Hemorrhages into the vesical walls are common.

As a result of injuries to the spinal cord the bladder may undergo a rapid dilatation and the walls at the same time have their nutrition interfered with. The urine rapidly collects, undergoes fermentative processes, and causes necrosis of the mucous membrane. This may be followed by perforation with fatal peritonitis and at times gangrene.

Tuberculosis of the bladder is generally secondary to tuberculosis of the epididymis, seminal vesicles, or prostate, or occurs as a descending infection from disease of the kidney. The disease manifests itself in the form of ulcers that are commonly located in the trigone, from which they may extend upward, involving the lower half of the bladder. The involved areas undergo cheesy degeneration and are frequently the seat of a deposit of urinary salts. There is usually a chronic cystitis present. Tuberculosis of the bladder is very much more common in men than in women. Primary tuberculosis is extremely rare and *syphilitic* ulcers are also very unusual.

Vesical calculi are very frequently encountered. They are composed of substances normally or abnormally present

in the urine. They may be present in great numbers, when they are small, like fine particles of sand, or singly as one large stone several centimeters in diameter and weighing as much as 1000 gm. The shape and the general characteristics of the calculi depend upon the material of which they are formed. The stones may be imbedded within the mu-

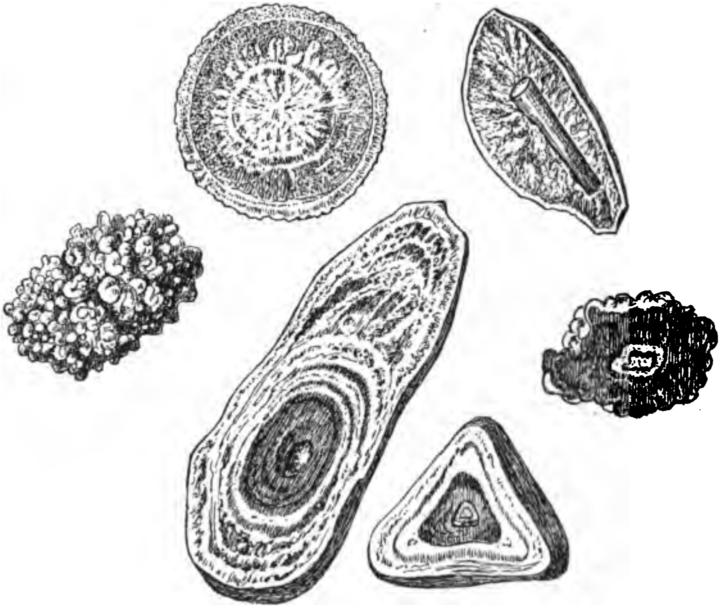

FIG. 155.—URINARY CALCULI (Orth).
Showing the nuclei from which they originate, the concentric laminæ by which they are formed, the radiating infiltration sometimes observed, and the various smooth and nodular surfaces.

cosa or they may lie free within the bladder. In the latter case the sides of the stones may be worn smooth by mutual contact.

The formation of a stone is generally considered to be due to the precipitation of the various salts about some desqua-

mated epithelium or foreign body. This is accompanied by a coagulation of albuminous material about the calculus and then another layer of mineral salts, giving a distinctly laminated appearance to the stone: Occasionally the nucleus may be a renal calculus that has passed through the ureter. It is usually of a different composition than those formed within the bladder.

Associated with the formation of calculi is generally a retention of urine.

These stones may be made up of uric acid or urates, of oxalate of lime, of phosphates, of carbonate of lime, or of various organic bodies, as cystin or xanthin.

The characteristics of the various calculi are as follows:

1. *Uric acid*, are less common in the bladder than in the kidney. Are small, round, hard, slightly granular surface, of a yellowish, reddish, or brownish color. They probably originate within the kidney.

2. *Urates*, of ammonium magnesium, often are covered by earthy phosphates. May be as large as a hen's egg, oval, smooth surface, pale in color, and laminated. If composed entirely of ammonium urate are seldom larger than a pigeon's egg, rounded but also flattened, friable, granular, and dull yellow.

3. *Calcium phosphate*, medium-sized, irregular surface, grayish in color, hard and brittle, or soft and crumbling if there is much triple phosphate present. Frequently form about small uric acid calculi.

4. *Triple phosphates*, large, irregular, grayish, soft, and friable.

5. *Carbonate of lime*, are rare, are small, white, and chalky.

6. *Oxalate of lime*, are round, brownish color, surface irregular and nodular, very hard, may be quite large. Are the *mulberry* calculi.

7. *Cystin*, unusual, small, oval, brownish or greenish, soft and waxy.

8. *Xanthin*, very rare, small brownish, smooth surface, and brittle.

Results of the vesical calculi are many. Their presence

may cause obstruction to the outflow of urine with subsequent dilatation of the bladder and its accompanying chronic cystitis. By pressure, atrophy and ulceration of the mucous membrane may take place with even perforation. Hypertrophy of the vesical walls occurs. There are frequent attempts at micturition, accompanied by straining and tenesmus, with frequently bloody urine. If long continued the obstruc-

FIG. 156.—PAPILLOMA OF THE BLADDER. × 35 (Ziegler). (Alk. Häm. Eos.) Section through a tuft.

tion may give rise to bilateral hydronephrosis or pyonephrosis if the infection extends upward.

Sometimes the calculus may become lodged in a pouch of the wall and become completely encapsulated.

Tumors.—*Polypoid* thickenings of the mucosa are quite frequently found in chronic inflammations of the bladder. *Fibromata* generally appear as small villous outgrowths, covered by epithelium. Are very vascular and may give rise to such considerable hemorrhage that grave or fatal anemia

ensues. Occasionally bits of the papillary growths may break off and be passed through the urethra or they may be large enough to cause obstruction. These tumors are benign, but there is a possibility of their becoming malignant. True connective-tissue tumors, particularly sarcoma, are rare. *Carcinoma* in the form of a squamous epithelioma is an infrequent primary tumor. It occurs as a cauliflower mass that frequently undergoes ulceration. The neighboring organs are generally involved by contiguity. Secondary *carcinoma* may follow malignant disease of the sexual organs, of the rectum, or of the prostate by direct extension. The bladder is very rarely the seat of a metastatic growth. Cysts very rarely are found.

DISEASES OF THE URETHRA

Malformations.—Occasionally the urethra may be absent, or the superior or inferior walls may be incomplete, giving rise to epispadias and hypospadias respectively.

Inflammation.—*Urethritis*, inflammation of the urethra, is nearly always an infectious condition resulting from the presence of the gonococcus. Non-specific urethritis may be due to injuries or to the entrance of pyogenic micro-organisms. In gonorrheal urethritis the mucosa of the anterior urethra is first involved. It becomes red and swollen and there is soon a formation of pus accompanied by a desquamation of the epithelium. In the pus cells as well as in the epithelial the characteristic organisms will be found. There is generally an infiltration into the deeper layers of the mucosa by the gonococci. The infection may extend to the posterior urethra, and involve the bladder, epididymis, prostate, seminal vesicles, and in women the bladder, vagina, uterus, and Fallopian tubes.

The inflammation in the urethra may subside without doing any damage or it may set up infectious processes in other parts of the body. Is not uncommon to have a gonorrheal ophthalmia, gonorrheal arthritis, an acute endocarditis, or pericarditis.

The acute form of urethritis is often followed by a *chronic* inflammation called *gleet*. The posterior urethra is the part generally involved and is accompanied by a very slight discharge of a thick transparent mucus seen in the morning. Not infrequently a fibrous cicatrix is formed in the urethra. This undergoing contraction gives rise to a stricture which is most commonly located in the membranous portion. If the narrowing is severe, the urine may be prevented from escaping, and consequently cause a dilatation of the bladder with hypertrophy and chronic cystitis. The ureters and kidneys may even be involved.

Injuries.—The urethra may be the seat of various injuries resulting from direct trauma, external or internal. If it is completely lacerated urine is able to escape into the tissues and rapidly give rise to a suppurative or gangrenous cellulitis. This may be very widespread, including the lower half of the abdomen and the upper part of the thighs. Fistulæ communicating with the vagina or rectum or opening externally may be formed.

Tuberculosis and **syphilis** are rare.

Tumors of the urethra are unusual except when secondarily involved by a neoplasm in adjacent structures, as in squamous epithelioma of the glans penis or in carcinoma of the prostate; in women in cancer of the cervix. The urethral *caruncle*, found in the meatus in women, is a fibrous angioma. Sarcoma, myxoma, and fibroma sometimes occur.

CHAPTER XXIII

DISEASES OF THE REPRODUCTIVE SYSTEM

MALE ORGANS

THE PENIS

Malformations of the Penis.—The penis may be absent, undeveloped, or, what is very rare, double. There may be lack of closure of the urethra on the dorsal surface, *epispadias*, or, on the under side, *hypospadias*. In the latter condition the cleft may extend posteriorly and separate the scrotum into two lateral halves. This is usually the condition in the cases of hermaphrodism. Epispadias may be associated with exstrophy of the bladder. The prepuce may be absent or, what is quite common, elongated and the orifice greatly narrowed; is termed *phimosis*.

Inflammation of the glans penis is known as *balanitis*, of the prepuce as *posthitis*, of the two together as *balano-posthitis*. Is generally the result of uncleanliness. Is a quite common complication in phimosis when the prepuce cannot be retracted. The smegma and urine undergo decomposition and set up an inflammation; infection, as in gonorrhea, may be the cause. Occasionally the prepuce when inflamed may be retracted behind the glans and unable to be drawn forward. Is called *paraphimosis*, and by its constriction may give rise to serious secondary conditions.

Injuries to the penis may give rise to hemorrhage or to rupture. If it becomes infected suppuration and gangrene may result. If the urethra has been lacerated extravasation of urine with its accompanying symptoms may occur. Injuries are likely to be more severe when the penis is in an erect condition.

Tuberculosis is rare. It appears as ulcerations on the glans with cicatrization and necrosis.

Syphilis generally makes its initial appearance on the penis as the true chancre.

Tumors of the penis are frequently found and are generally epithelial in structure. The *papilloma* or *condyloma* appears as a hard, rough, cauliflower-like growth upon the glans penis or prepuce. Is composed of vascular connective-tissue villosities covered by squamous epithelium. *Carcinoma* usually occurs in the form of the squamous epithelioma arising from the glans or the prepuce. It is generally warty and prone to ulcerate. Large areas of the penis may be destroyed and metastases to the neighboring inguinal lymph-nodes occur. The connective-tissue tumors are rare.

Scrotum.—Is quite frequently the seat of epithelioma in chimney-sweepers and paraffin-workers. *Elephantiasis* is common in the East and in many cases is due to the filariæ. The subcutaneous tissue is greatly increased, so that an extreme enlargement may occur. *Dermoid cysts* are occasionally met with.

THE TESTICLES

Malformations.—One or both testicles may be absent or hypoplastic. *Cryptorchia* is a condition in which one or both testicles instead of descending into the scrotum remain within the abdominal cavity or in the inguinal canal. Occasionally the testicles may not descend till puberty. The undescended testicles are usually small and imperfectly developed, and are not uncommonly the seat of a sarcomatous proliferation.

Atrophy of the testicle occurs in senility and after chronic inflammations. The organ is small and dense, is dark in color, and is incapable of spermatogenesis, the epithelium having undergone a fatty degeneration.

Hypertrophy has been noticed as a compensatory change following the removal of one testis and is characterized by an increase in size of the seminiferous tubules.

Fatty degeneration is quite frequently observed as a

result of pressure from tumors or from other pathologic conditions within the testicle.

Inflammation of the testes—*orchitis*—and of the epididymis—*epididymitis*—are commonly encountered. The two may occur together or alone. If the surrounding tunica albuginea is involved the condition is called *periorchitis*.

The inflammation may be due to traumatism or to infection, the latter usually resulting from the extension of a gonorrhea. In typhoid fever, scarlet fever, syphilis, smallpox, and mumps the testicles are occasionally the seat of inflammatory changes, as a result of hematogenous infection. The traumatic and gonorrheal processes generally involve the epididymis only.

Orchitis may be acute or chronic. In the acute form the testicle is swollen, hard, and very painful on account of the organ being inclosed within the fibrous tunica albuginea. Microscopically there is seen a marked round-cell infiltration between the tubules. The epithelial cells degenerate and desquamate. The condition may terminate in suppuration; and if the tunica is broken through, the testicular substance may protrude and form a fungous condition. The organ may, on the other hand, entirely recover.

Chronic orchitis usually follows the acute variety or as a complication of syphilis. In it there is a great hyperplasia of the intertubular connective tissue with subsequent contraction, atrophy, and degeneration, the testicle becoming very dense.

In *epididymitis* that structure becomes much swollen and painful and is usually associated with a serous exudation into the tunica vaginalis.

Tuberculosis generally is primary in the epididymis and secondarily involves the testicles. The infecting organisms may gain entrance either through the circulation or from the urethra through the vas deferens. In the latter form there has generally been a pre-existing tuberculosis of the seminal vesicles, prostate, or bladder.

The condition is, as a rule, secondary to pulmonary tuberculosis, small tubercles develop, these increase in size, coalesce,

and form quite large caseous masses which may break down and rupture externally.

Syphilis, either acquired or congenital, may give rise to changes in testicles and epididymis; the testicle usually being involved secondarily. There is generally an intertubular round-cell infiltration with induration and degeneration of the tubular epithelium. Gummata sometimes form and undergo a caseous degeneration with subsequent cicatrization.

Leprosy of the testicle in the form of nodular formations, with degeneration and atrophy of the tubules, has been noted.

Tumors.—*Fibroma*, *lipoma*, and *myxoma* are sometimes encountered. *Chondroma* and *rhabdomyoma* have been described. *Sarcoma* in all varieties occurs in the testicle, less commonly in the epididymis. Secondary changes frequently occur, and cysts of various sizes may form. Combinations of the sarcoma with chondroma, lipoma, fibroma, etc., are quite common.

There have also been described tumors of the testicle that contain areas resembling the chorioepitheliomata that are found in women.

Adenoma is rare; when present it is generally associated with carcinomatous proliferation of the epithelium. *Carcinoma* is not unusual, and though usually medullary in type may be scirrhus. Is frequently associated with cystic dilatations of the tubules. Various degenerations, as mucoid and colloid, are quite commonly seen. Although the tumor originates within the cells of the seminiferous tubules of the testicle the epididymis and vas are soon involved, the entire organ being transformed into carcinomatous tissue.

Cysts.—*Spermatocele* is the term applied to a cystic dilatation of a seminal tubule, usually at the head of the epididymis. It may be quite large, containing up to 350 c.c. of a watery, slightly turbid fluid in which spermatozoa, either active or dead, may be found. *Retention* cysts may occur as a result of inflammatory changes, or to obstruction of the tubules by some new growth. Are spoken of as galactoceles when the contents are milky in color. *Dermoid* cysts are rarely found.

Vaginitis testis, or **periorchitis,** is an inflammation of the tunica vaginalis. It occurs as a result of inflammation of the testicle or epididymis, in the course of various infectious diseases or in consequence of traumatism. The most common form is the *serofibrinous* variety in which there is an accumulation of serous fluid within the tunica vaginalis, giving rise to a *hydrocele.* The process may continue slowly and the tunica be tremendously distended by a clear straw-colored fluid. In acute cases the fluid may be purulent or hemorrhagic.

If the hydrocele has continued a long time the tunica vaginalis becomes much thickened and the testicle and epididymis frequently atrophic.

THE SEMINAL VESICLES

Vesiculitis, or inflammation, generally follows an attack of gonorrhea or of prostatitis. The tubules become dilated by a mucopurulent exudate, are congested and tender, and in chronic inflammation, there may be a connective-tissue formation. This through contraction may give rise to various deformities. Obstruction to the tubules as they enter the prostatic tissue causes the dilatation.

Tuberculosis may be primary or secondary to tuberculosis of the pulmonary or genito-urinary tracts. The bacilli gain lodgment by means of the blood-vessels or lymphatics. They are present in the semen and when contained within the vesicles infect them.

Tumors are seldom primary, usually being secondary to carcinoma of the prostate or rectum.

THE PROSTATE GLAND

Atrophy of the prostate is common in old age, the gland becoming smaller through degeneration of the epithelium with contraction of the fibrous tissue.

Hypertrophy also frequently occurs in old men. The entire gland or any one of its lobes may increase in size. Although the gland is composed of two lobes connected by a narrow isthmus the hypertrophy can involve the isthmus

FIG. 157.—HYPERTROPHY OF THE MIDDLE LOBE OF THE PROSTATE (White and Wood).
A, Middle lobe of prostate; *B*, urethra.

alone and cause a great increase in size. This median enlargement is the most important, as it is the one in which there are severe clinical symptoms. By the hypertrophy of this portion the opening to the urethra is obstructed and retention of urine occurs. This may at first merely give rise to increase in the thickness of the muscle-fibers and dilatation

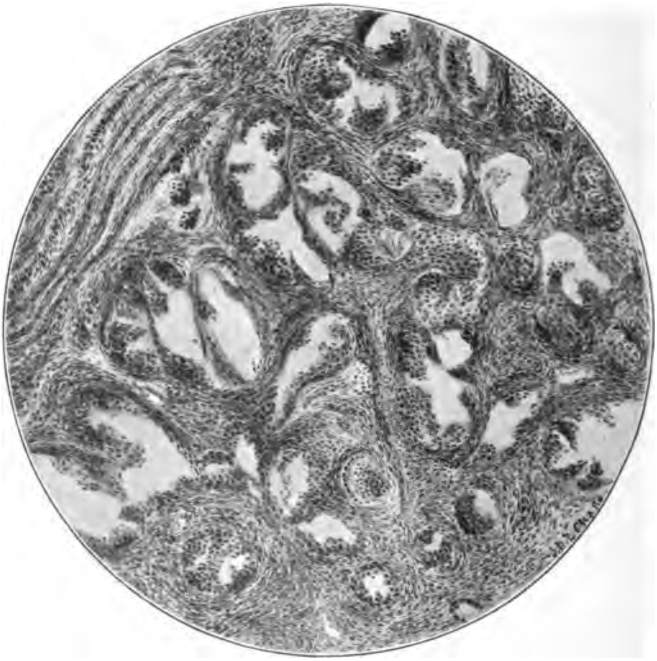

FIG. 158.—HYPERTROPHY OF THE PROSTATE GLAND (McFarland).

of the bladder. Subsequently infection takes place, the urine decomposes, and the bladder is no longer able to expel the urine. Pyelitis and pyelonephritis may follow.

Microscopically the enlargement is due either to a glandular increase or to a hyperplasia of the fibrous connective-tissue

stroma. In the latter case there may be more or less widespread atrophy of the tubules. In the glandular form the appearance closely simulates that of an adenoma.

The enlargement may result from a chronic posterior urethritis or a long-continued congestion.

Prostatitis, inflammation of the prostate, is nearly always secondary to a posterior urethritis, but may follow injury to the perineum. In the acute infectious form there is a desquamation of the glandular epithelium, with collections of pus in the acini, and a round-cell infiltration of the interstitial tissue. There may be numerous foci of suppuration scattered throughout the tissue. Large abscesses may form and these generally evacuate into the urethra. If further infection of the surrounding tissues does not occur cicatrization and recovery take place.

With the opening into the urethra there may be an extravasation of urine with phlegmonous inflammation of the pelvic tissues.

If the abscesses do not rupture, they may be absorbed or become inspissated, encapsulated, and calcified.

Concretions are quite frequently found in the prostatic alveoli in old men. They are generally numerous and vary in size from the microscopic to those large enough to be seen with the naked eye. They are round, translucent, colorless bodies that show a distinct concentric arrangement. The older ones are of a slight brownish tinge. They are frequently spoken of as *corpora amylacea* on account of their so often giving a starch reaction, coloring blue or a mahogany-brown color with iodin. They may, however, not stain at all. As they become larger, lime-salts are commonly deposited around them. Occasionally the concretions may be so large as to cause the ducts to dilate. At times they escape into the urethra and are passed out with the urine.

Tuberculosis of the prostate is generally secondary to tuberculosis of the other genito-urinary structures, particularly of the vas deferens and epididymis. Throughout the gland there are caseous masses varying in size. These may become encapsulated and calcified or may rupture into neighbor-

ing tissues. Primary tuberculosis sometimes occurs as a hematogenic infection, but is quite rare.

Tumors of the prostate are not common. *Sarcoma* and *adenoma* are very rare. *Carcinoma* is more frequent, but even it is unusual either as a primary or a secondary growth. It may occur in rather young individuals and appears as a nodular yellowish mass that projects into the bladder and urethra. It soon breaks down, leaving an ulcerated surface. Extension usually involves the bladder and rectum, but metastases to the inguinal nodes or more distant organs frequently take place; death rapidly ensuing.

Cysts are very rare, occasionally arising from remnants of Mueller's ducts or from obstruction to the ducts.

COWPER'S GLANDS

These become involved in the course of inflammations of the prostate gland or of the urethra. The glands become hyperemic, enlarge, and may suppurate. The abscess may rupture into the urethra or externally, in either case giving rise to a fistula. The duct may become narrowed as a result of inflammation and form a retention cyst.

THE FEMALE ORGANS

THE OVARIES

Malformations.—The ovaries may be hypoplastic or occasionally one may be absent, seldom both. An ovary may be much displaced, sometimes being found in the inguinal canal or in the labium majus. It may also be displaced as a result of a change of position in the uterus or from pressure or adhesions.

Circulatory Disturbances.—*Active hyperemia* may be either pathologic or physiologic; in the first as a beginning inflammation or in the latter during the menstrual period.

Chronic hyperemia is found in chronic heart disease or as a result of some localized obstruction.

Hemorrhage takes place when a follicle is ruptured. The blood escapes into the follicle after the ovum has been cast

off and at the same time the cells lining the follicle proliferate. They soon undergo fatty degeneration, forming the *corpus luteum* of menstruation. The blood is finally absorbed, the cells break down, and organization takes place, leaving a small scar. When impregnation has occurred the corpus luteum is considerably larger than the above, and there is a more marked proliferation of the follicular cells. Instead of rapidly organizing it may persist even to the end of pregnancy. It contains a translucent gelatinous substance and little blood. The luteal cells are arranged in peculiar fan-like folds.

Oöphoritis, or *inflammation* of the ovaries, is generally secondary to an inflammatory condition of the Fallopian tubes or of the peritoneum. Is generally due to the presence of pyogenic organisms which may infect the ovary by direct contact, as in peritonitis, or be carried in the blood- or lymph-vessels.

The ovary is much enlarged and congested and round-cell infiltration is common. Small abscesses may appear as minute yellowish points. Occasionally larger collections of pus form and these may rupture into the peritoneal cavity or into a loop of intestine. Generally the inflammation quiets down with absorption or inspissation of the abscesses and terminates in connective-tissue formation, *chronic oöphoritis*. As a gradual transformation of the ovary into fibrous tissue is a normal process as the person advances in age, the change cannot always be attributed to inflammatory processes.

Adhesions frequently follow oöphoritis and may cause serious trouble by their presence.

Tumors of the ovary are, as a rule, cystic in character.

Small follicular cysts may occur singly or multiple, as a result of the failure to discharge the ovum, with subsequent enlargement of the follicle. They may become as large as a man's fist and contain a thin or jelly-like fluid that is usually clear but which may be discolored by the presence of blood. Such cysts are lined by a single layer of flattened epithelium, and are formed within the ovarian tissue.

The neoplastic cysts differ from the follicular in that the dilated spaces are surrounded by fibrous tissue that supports

a vascular basement membrane upon which the cells rest. The epithelium is usually columnar and rarely is ciliated. These cysts are probably developed from Pflüger's tubes, and represent a *cystic adenoma.*

Instead of being single they are multilocular, and may be divided into two groups—the simple cystoma and the papillary cystoma. The material contained within the cysts is usually clear and gelatinous, if there has not been an admixture of blood. Although this substance closely resembles mucin it is not precipitated by acetic acid, consequently it is known as *pseudomucin.*

The *simple cystoma* is a benign growth and retains to some extent a glandular arrangement, in that there are formed acini lined by epithelium. It is usually multilocular, although in many instances the septa between the acini have been broken. The contents are usually thick and viscid on account of the pseudomucin present. This substance is less frequently found in the papillary cystoma.

At times the proliferation of the epithelium may take on a malignant tendency and give rise to a carcinomatous degeneration. This is more frequent in the papillary variety.

The *papillary cystoma* are generally bilateral and probably originate from the paroöphoron. From the inner surface of the cyst there extend papillary outgrowths covered by a stratified layer of ciliated columnar epithelial cells, many of which are of the goblet type. The fibrous framework is less marked, and concentric calcareous bodies (psammoma bodies) may be found within it. The substance in these cysts resembles that found in the simple form, except that there is a less amount of pseudomucin.

This form is much more inclined to undergo a secondary malignant degeneration than is the simple cystoma. The growth may be so rapid as to cause the wall of the cyst to rupture and the papillary structures project on the surface, giving rise to a cauliflower-like mass.

Dermoid cysts are more commonly found in the ovaries than in any other part of the body. They may be very small or large, and though generally unilateral may occur in both

ovaries. Their structure and origin has already been described. Their origin has been explained as a *fœtus in fetu*, or as a result of parthenogenesis of an unfertilized ovum.

Tumors.—*Carcinoma* of the ovary is nearly always a primary growth. It is glandular in character and generally undergoes a mucous degeneration. It usually gives a wide-

FIG. 159.—PAPILLARY CYSTOMA OF THE OVARY. × 150 (Ziegler).

spread metastasis along the peritoneum. Is not infrequent in childhood, and is rapidly fatal.

Fibroma may be found singly or multiple. They probably originate from the scars formed in the organization of the corpora luteii. Combination with sarcoma, fibrosarcoma, sometimes occurs. *Myofibroma* are also met with. *Chondroma* is rare. *Sarcoma* is rare, but may occur as a spindle

cell or, more rarely, as a round-cell variety. Myxomatous degeneration is common. Metastasis is unusual, and the malignancy of these growths is slight. If there are many glandular structures present the neoplasm is called an *adenosarcoma*. *Angiosarcoma* occasionally occurs. ***Endothelioma*** is unusual.

THE FALLOPIAN TUBES

Malformations of the tubes are not frequent. Are usually associated with abnormalities of the uterus. They may occupy unusual positions as a result generally of adhesions.

Hyperemia of the tubes occurs in the early stage of inflammation and during menstruation. *Hemorrhage* is rare, except from a rupture of the tube in an ectopic pregnancy.

Salpingitis or inflammation of the tube is always the result of infection by micro-organisms gaining entrance from the uterus. It may be acute or chronic, and the most common cause is the gonococcus. Is also generally present in puerperal infections.

In the *acute* form the mucous membrane of the tube shows a catarrhal inflammation with an accompanying exudation. This latter varying according to the severity of the inflammation, being mucous, purulent, or hemorrhagic. There is a marked round-cell infiltration of the mucosa, and many of the epithelial cells may desquamate.

The exudate escapes from the fimbriated end of the tube, and sets up an inflammation of the adjacent tissues with the formation of adhesions. If the uterine end becomes obstructed the exudation may be retained. If the contents are purulent a *pyosalpinx* is formed; if much blood is present, a *hematosalpinx;* and when serous, the condition is called a *hydorsalpinx*. If the secretion of fluid continues the tube may become much dilated with any of the above contents. The walls will become thinner and rupture may occur. The contents may be discharged into the abdominal cavity, into the intestine, or be walled in by adhesions. If rupture occurs during the acute stage general peritonitis will usually result.

If, however, the condition has been chronic the exudation is nearly always sterile on account of the death of the infecting bacteria.

In *chronic* salpingitis there is a hyperplasia of the connective tissue and muscularis; it is generally secondary to an acute infection. The tube-walls become much thickened, and adhesions to the outer surface are present. They may cause considerable distortion.

The contents of the tube may gradually be absorbed or calcareous material may be deposited.

Tuberculosis of the tubes is unusual; it may be either primary or secondary. The general appearance is similar in both forms. On the surface are numerous scattered miliary tubercles, and throughout the walls of the tube are minute caseous areas. Dense adhesions are commonly formed, and the organs are firmly bound down to neighboring structures. This condition may be associated with gonorrheal salpingitis. The uterus may become secondarily involved by the discharge into it of infected material from the tubes.

Syphilis is very rare, but has been found in the form of gummata and connective-tissue hyperplasia.

Tumors are not very frequent. *Fibroma, myoma*, and *fibromyoma* and *lipoma* have been described. *Papilloma* of the mucous membrane occasionally form and they are probably the starting-point of primary carcinoma. Secondary carcinoma is the result of extension from uterine involvement. *Sarcoma* and *syncytioma malignum* are sometimes found.

Cysts of the Fallopian tubes are generally present, as hydrosalpinx, a consequence of obstruction. Small cysts attached to a somewhat long and narrow pedicle are known as *hydatids of Morgagni.*

EXTRAUTERINE PREGNANCY

If there is any interference with the entrance of the impregnated ovum into the uterus an extrauterine development takes place. This may be within the ovary, between the

tube and ovary,—*tubo-ovarian,*—or, what is most common, within the tube—a *tubal* or *ectopic* pregnancy.

The chorionic villi are formed, deciduæ develop, and a placenta is evolved. At the same time there is commonly a decidua formation within the uterine cavity. As the embryo increases in size the walls of the tube become gradually thinner. By about the third month the tube generally ruptures. This may take place within the layers of the broad ligament, into the peritoneal cavity, or into the uterus. In any case there are severe symptoms of pain and shock and large internal hemorrhage occurs. It is very dangerous if the rupture has taken place at the placental site. Death may result from the loss of blood or from a peritonitis.

If the ovum has died the fetus may degenerate and become infiltrated with lime salts, forming a *lithopedion.*

If the impregnated ovum lodges somewhere on the peritoneum, we have an *abdominal pregnancy.* A similar condition is present at times when the ovum has escaped from a ruptured tube. In such instances the placenta usually remains within the tube. Peritonitis commonly ensues, the fetus perishes, and a lithopedion may form.

THE UTERUS

Congenital malformations are not infrequent and are the result of imperfect development of the Müllerian ducts. These ducts are two parallel tubes that normally unite in their long axis, forming in this way the uterus. There may be marked hypoplasia of the uterus and vagina, with very imperfect development of the tubes and ovaries. By failure of fusion of the ducts the uterus may contain two cavities, and if it extends downward divide the vagina into two canals.

Atresia or *stenosis* of the os uteri may be either congenital or the result of inflammatory conditions. On account of the obstruction the uterine cavity may become *dilated* by the retention of fluids. If by menstrual discharges is known as *hematometra;* by seromucous secretion, *hydrometra;* if decomposition occurs and gas is formed it is then a *physometra;* when pus is present, is a *pyometra.*

Rupture of the uterus may result from the retention of fluid with gradual thinning and degeneration of its walls. It generally happens as an accident during pregnancy or labor. There may be some diseased condition, particularly malignant, of the muscle, or the wall may give way on account of too great contraction of its fibers. If the tear does not extend all the way through the wall, it is an incomplete rupture; is complete whenever the serous covering is involved. The condition is associated with shock, and generally very severe and frequently fatal hemorrhage. If death does not result from the loss of blood, it usually follows from peritonitis. Sometimes the wound will cicatrize, the fetus degenerate and be discharged through fistulæ, and the patient recover.

In rupture the tear begins, as a rule, just above the cervix on the inside and extends in the direction of the fundus. If the uterus has been perforated by an instrument, the larger opening of the wound is on the outer surface, the opposite to what occurs in rupture.

Malpositions of the Uterus.—Normally the uterus is in a position of slight anteflexion and anteversion. The common displacements are either forward or backward, as the broad ligaments prevent lateral changes. In pathologic *anteflexion* the uterus is greatly flexed or bent, allowing the fundus to fall forward and downward. As a result the uterine cavity is obstructed and the menstrual fluid retained, giving rise to dysmenorrhea. In *anteversion* the fundus of the uterus falls forward and the cervix is displaced backward without a change in shape. In *retroflexion* the uterus is bent backward at an angle, the fundus falling downward and backward toward Douglas's pouch. *Retroversion* refers to a bending backward of the uterus without any change in the shape of the organ. Although they may occur separately, retroflexion and retroversion are generally associated. These deformities may be due to pressure from above, from the presence of new growths, from tight clothes, or to the presence and contraction of inflammatory adhesions. They may also be brought about by disease of the uterus itself.

The uterus may be elevated as a result of the presence of

tumors within the pelvis or of the contraction of adhesions dragging the organ upward. The opposite condition, *prolapse* of the uterus, or *procidentia*, is comparatively frequent. It is apparently due to a loss of tone in the structures supporting the organ, as in a torn perineum, or to an enlargement of the uterus. As it descends the vagina is slowly invaginated. According to the extent of the prolapse three degrees of severity may be considered. If the descent is slight and the uterus does not leave the pelvis, it is a *simple* prolapse; if the organ is not entirely out of the pelvis, it is a *partial* prolapse; if the uterus has descended to the vulva and discloses the vaginal walls, it is a *complete* prolapse or *procidentia*. In this latter the rectal and vesical walls are also dragged down, causing a *rectocele* and a *cystocele*. *Inversion* is a condition in which the uterus is more or less completely turned inside out. It occurs during labor, from large polyps or from localized pressure on the fundus. This condition is often accompanied by prolapse.

Stenosis of the cavity of the uterus may result from various inflammations or may be congenital. As a result of the blocking of the outlet *dilatation* of the uterus not infrequently occurs.

Circulatory Disturbances.—*Active hyperemia* is normally present during menstruation and pregnancy, and is similar to what takes place in pathologic conditions. The mucous membrane becomes much congested and swollen and there is a round-cell infiltration between the glands, which are somewhat increased in length. There is probably little or no desquamation of the surface epithelium. Serum is secreted and this may be hemorrhagic or purulent according to the diapedesis of erythrocytes or the emigration of leukocytes.

Passive hyperemia may be part of a general stasis, but is especially marked in severe malpositions or when neoplasms press upon the venous plexuses. The uterus is enlarged, dilated veins are seen on the outer surface, the mucosa is dark red, and the condition generally terminates in a chronic hyperplastic endometritis.

Hemorrhage may be normal, as in menstruation, or pathologic. The blood may be within the uterine cavity, in the uterine walls, or outside in the peritoneal cavity. When the menstrual period is lengthened and more blood than is normal is lost, it is known as *menorrhagia;* if the hemorrhage is between the menstrual periods, *metrorrhagia.* Normally the mucous membrane remains intact, but under certain pathologic conditions large masses of endometrium may be discharged; this is called *dysmenorrhea membranacea.*

In hemorrhage into the peritoneum the blood usually collects in Douglas's pouch. It may be derived from a ruptured tubal pregnancy, a hematosalpinx, or ruptured varicose veins of the broad ligament. The resulting hematoma may be large or small, and it may become absorbed or be encapsulated. Inflammation may occur with the formation of adhesions between the uterus and rectum. Occasionally the blood may escape by perforations into the rectum or vagina. Death may follow the loss of blood.

Atrophy occurs normally in old age, or as a consequence of the removal of the ovaries. The uterus becomes much smaller, dense, and pale, and the blood-vessels show an obliterative arteritis. The endometrium is also greatly reduced in thickness and the greater part of the glands is lost.

Following childbirth the uterus under normal conditions at first rapidly atrophies, then decreases more slowly. By the end of the fourth month it has usually regained its normal size. This process of involution consists essentially in a fatty atrophy of the muscular fibers, which decrease not only in size but also in number.

Hypertrophy may involve the entire uterus, as in the enlargement in pregnancy or in chronic congestion and inflammation. Local hypertrophy generally involves the cervix, which becomes much elongated and may present itself at the vulvar orifice.

Fatty degeneration other than the above is unusual, but has been found in typhoid fever, cholera, and in phosphorous poisoning.

Amyloid degeneration is rare; either the arteries or the muscle may be alone involved.

Inflammation of the uterus, if of the outer serous surface, is a *perimetritis;* of the muscular coat, *metritis;* of the lining mucous membrane, *endometritis.*

Perimetritis may result from puerperal infection, or be a part of a general or local peritonitis. In the acute form there may be a layer of pseudomembrane over the uterus and even involving neighboring structures. The process soon becomes chronic with the formation of adhesions. *Parametritis* is an inflammation of all the structures of the uterus accompanied by a cellulitis of the broad ligament and pelvic tissues. Usually occurs as a result of puerperal infection.

Metritis may be acute or chronic. The *acute* form generally occurs during the puerperium, but may be the result of gonorrheal infection. The uterus is much enlarged, congested, soft, and infiltrated with leukocytes. Occasionally small abscesses may form. The muscle fibers degenerate, thrombosis of the uterine sinuses and veins is quite common, and gangrene sometimes occurs.

Chronic metritis usually follows the acute form, or is the result of delayed involution of the uterus. There is a round-cell infiltration along the blood-vessels, the connective tissue increases and by contraction causes the muscle-fibers to atrophy. The uterus finally becomes small, pale, and dense. The entire organ is commonly involved, but occasionally the cervical portion is alone affected—it becomes enlarged, congested, and soft at first but afterward indurated.

Acute endometritis is usually the result of infection by pyogenic organisms or by the gonococcus. It may be found in the course of certain infectious diseases, as typhoid fever, cholera, scarlet fever, and diphtheria. The mucous membrane is very hyperemic and swollen, and there is quite extensive desquamation of the epithelial cells. Small hemorrhagic areas are seen, and there is a marked mucopurulent exudate. There are round-cell infiltration and necrosis of the epithelium; the formation of a pseudomembrane may occur. In gonorrhea the cervical portion is the usual seat, in other infections the fundus.

Chronic endometritis may follow the acute variety, or result

from general debility, local congestion and malnutrition, or from the irritation of tumors.

The mucous membrane is swollen, there is some round-cell infiltration and a more or less marked mucopurulent secretion. As the condition persists there is an increase in either the interstitial tissue or the uterine glands. In *endometritis glandularis* the increase in the size and number of the glands is the striking feature. The glandular hyperplasia may be so

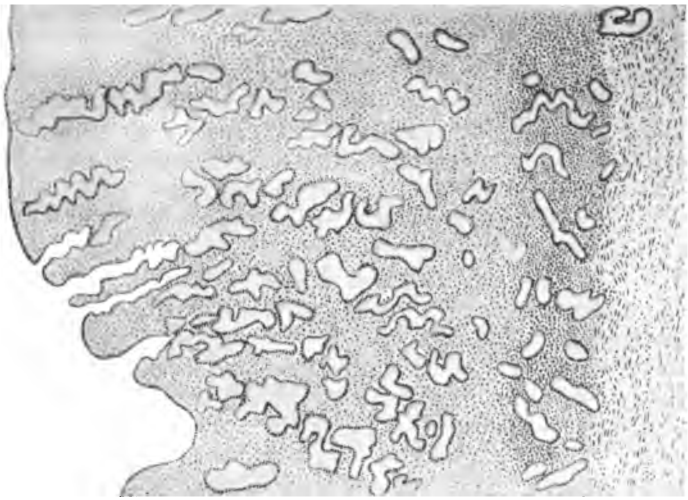

FIG. 160.—CHRONIC GLANDULAR ENDOMETRITIS. × 40 (Dürck). Uterine glands greatly proliferated, lengthened, and convoluted.

great as to closely resemble an adenoma. In *endometritis interstitialis* the glands are much fewer than normal, and there is a round-cell infiltration and hyperplasia of the interglandular connective tissue.

Atrophy may occur in late stages of chronic endometritis and the glands be displaced by connective tissue. In this process the openings of the acini, particularly of the Nabothian

glands of the cervix, may become obstructed and give rise to small retention cysts.

Chronic endometritis may give rise to chronic metritis or by extension involve the tubes.

Ulceration or *erosion* of the cervix is very common, and results from endometritis and from lacerations. There is a destruction of the superficial epithelium with exposure of the deeper tissues. Occasionally there may be a rapid *phagedenic* ulceration with great destruction of tissue extending to the bladder and even to the rectum. Has been thought to be carcinomatous, but microscopic examinations have been negative.

Lacerations of the cervix result from childbirth; they may be simple, double, and multiple or stellate. They are very slow in healing and the exposed surfaces become covered by granulations. Fibrous connective tissue is usually formed, and the part may become very dense and hard.

Tuberculosis of the uterus is nearly always secondary to that of the tubes. The endometrium is usually affected and presents either a nodular or a diffuse infiltration. At times the endometrium may be completely transformed into a caseous mass.

Syphilis of the uterus is rare, but may occur as a chancre upon the cervix or as gummata.

Tumors.—*Fibroids.*—These tumors are the most common of those of the uterus. Although spoken of as fibroma, they nearly always contain a large amount of involuntary muscle, so the term *fibromyoma* is the more correct. They occur very frequently in negroes. They are classified according to their situation into: *mural*, *intramural*, or *interstitial*, when occurring within the muscular body of the uterus; *submucous*, when beneath the endometrium; and *subperitoneal*, when beneath the peritoneal covering. The tumors may be single or multiple, and their size varies from a pea to one weighing fifty pounds. The largest are the subperitoneal, as their growth is practically unlimited.

The density of the tumors depends upon the amount of fibrous tissue present. They are generally encapsulated.

The blood-supply is poor, so degenerations are common. These usually begin in the center of the tumor, and the most frequent form is calcification. If the tumor has been a pedunculated one, the pedicle may become twisted and necrosis set in. Fibromata may be associated with lipoma, myxoma, or sarcoma.

Fibroid tumors, although of the benign type, may give rise to severe symptoms on account of exerting pressure upon neighboring structures. The submucous type is often associated with hyperemia and hemorrhage from the endometrium or from a degenerated growth. Infection with necrosis and gangrene may take place. Labor may also be interfered with by the presence of such tumors.

Sarcoma of the uterus usually originates within the connective tissue between the muscle-fibers and about the vessels or occasionally from the muscle cells—*myoma sarcomatodes*. It may also arise within the submucous tissue. The myometrial sarcoma is generally spindle-cell in character; is grayish-white and soft; the endometrial is commonly round celled. *Angiosarcoma* is rare, and the so-called adenosarcoma is probably nothing more than an inclusion of the pre-existing endometrial glands.

A peculiar tumor occurring in early life is the edematous papillary sarcoma of the cervix. It is composed of a mass of soft, grayish, grape-like structures, that microscopically are made up of myxomatous round and spindle cells. There are also found epithelial tubules, areas of cartilage, and both smooth and striated muscle-fibers. Is quite malignant.

Papilloma appear on the cervix as rather small, cauliflower-like growths, composed of connective-tissue villi covered by many layers of squamous epithelium. Venereal warts are sometimes found upon the cervix.

Adenoma as such occur as polypoid projections from the mucous membrane, or as a glandular hyperplasia of the endometrium. They are benign.

Malignant adenoma, or *adenocarcinoma*, usually arises in the fundus of the uterus, upon the posterior wall. It is characterized by the tendency of the glands to invade the

uterine muscle and by the epithelium breaking through the basement membrane. Quite frequently the epithelium proliferates so rapidly that the acini become completely filled with cells, the glandular character is lost, and the tumor assumes a typical carcinomatous structure. Metastasis is unusual; the destruction is mainly local. The invasion and destruction of the muscle progresses until the bladder and the rectum may become involved (see Fig. 49).

Carcinoma is usually an adenocarcinoma and the progress is practically similar. There is rapid infiltration with extensive ulceration. The vaginal walls and the tissues in the neighborhood of the cervix become involved. The neighboring lymphatic nodes are frequently the seat of metastases.

Squamous epithelioma of the cervix is the commonest type of malignant tumor. In many cases it probably begins as a papilloma. There is soon developed a tendency of the cells to infiltrate the surrounding tissues and to grow superficially as a cauliflower mass. The growth extends downward, involving the vagina; extensive ulceration, accompanied at times by severe hemorrhage, occurs, and there is an extremely foul discharge. The tumor extends in all directions, and may perforate into the bladder or rectum or into the peritoneal cavity, giving rise to fatal peritonitis.

In old people squamous epithelioma may occur in the body of the uterus when metaplasia of the columnar epithelium has taken place.

Syncytioma malignum, or chorio-epithelioma, is a peculiar malignant tumor developing from embryonal tissue. The greater part of the cells are supposed to be derived from the syncytium. Is a rare form of growth.

Cysts of the uterus may result from a liquefaction necrosis of a fibromyoma, or from the obstruction of the Nabothian follicles. Dermoid cysts are occasionally found. Parasitic cysts due to the cysticercus and echinococcus have been described.

THE VAGINA

Malformations.—The vagina may be imperforate in its entire length or only partially. There may be a septum

dividing the canal in two; such a condition is usually associated with a double uterus. Stenosis is seldom congenital; is generally secondary to some ulcerative condition.

When there has been a loss of support, as from a torn perineum, there may be a prolapse of the vagina, usually of the anterior wall. As the tissues relax the bladder is gradually involved; it is dragged downward and appears as a bulging of the vaginal wall,—a *vaginal cystocele.* If the posterior wall prolapses and drags in the rectum, it is known as a *vaginal rectocele.*

Wounds may result from the introduction of foreign bodies, from coitus, or from injury during childbirth. If the injury or destruction to the part has been severe, *fistulæ* may be established between the vagina and neighboring structures. Communication between the bladder is known as a vesicovaginal *fistula;* with the urethra, *urethrovaginal;* with the rectum, *rectovaginal.* Severe secondary inflammations may result from infection by urine or feces.

Inflammation of the vagina, *vaginitis* or *colpitis*, may be due to injury, as from hot douches, to the presence of foreign bodies, to the oxyuris, or to gonorrhea. In mild attacks there is a simple catarrhal inflammation, the mucous membrane becomes reddened, swollen, and covered by a slight alkaline mucopurulent secretion. In the gonorrheal form the reactions are more severe, the discharge is more purulent, and the cervix and urethra are generally involved. Occasionally when the inflammation is of a very high grade the mucosa may be exfoliated, almost as a cast of the vagina. A *pseudo-membrane* may be formed in the course of pneumonia, pyemia, and other infectious diseases. The mucous surface is covered by a dirty grayish pseudo-membrane that is eventually cast off, leaving quite extensive ulcerations. This may be followed by necrosis of the vaginal walls.

Chronic vaginitis or *leukorrhea* may follow acute attacks or be the result of constitutional disturbances. Is commonly known as "the whites," on account of the presence of a thick, creamy exudate, acid in reaction. The mucosa is reddened and swollen, and resembles the condition seen in acute

vaginitis. The discharge at times is thinner and contains less pus. Sometimes there may be marked thickening of the vaginal mucosa with very little discharge.

Tuberculosis of the vagina is secondary to similar disease of either the uterus—in which case it appears as rounded ulcers—or if of the vulva it is in the form of lupus.

Syphilis of the vagina is unusual. It may appear as a chancre, a mucous patch, or in the form of ulcers. Gummata may form and through regeneration give rise to distortion of the vagina as the scar-tissue heals.

Tumors.—*Fibromata* or *fibromyomata* are found in the submucous and muscular layers as either projecting nodules or as polyps. *Sarcomata* are rare. *Papillomata* are fairly common. *Carcinoma* is usually secondary to cancer of the cervix or of the rectum. When primary, is usually of the squamous epithelioma variety and cauliflower-like in its growth.

Cysts of the vagina are usually the result of obstructions of the follicles. They are generally small and may be single or multiple. Some of the larger cysts may develop from remains of the Wolffian or Müllerian ducts. May also be the result of lymphangiectasis.

THE VULVA

Wounds are particularly common as a result of childbirth. They generally occur as lacerations of the posterior fourchette and may extend not only into the perineum but into the rectum. If the damage has been very severe, extensive necrosis and even gangrene may follow. Severe hemorrhage is also not uncommon, forming a hematoma within the labia. If comparatively mild infection takes place, abscesses may form.

Hyperemia may be due to acute inflammatory conditions or occur as a result of local irritation, as from the oxyuris. Is accompanied by increased exudation. Passive hyperemia may be a part of a general venous stasis or the result of some local obstruction to the outflow of blood.

Inflammation of the vulva may be the result of many conditions: uncleanliness, gonorrhea, or injuries. The parts

become reddened, swollen, edematous, and are accompanied by a marked exudation that may be mucoid, serous, or purulent, or any combination of the three. Pseudo-membrane may form and gangrene also may occur. Abscesses may be due to infection or to extension.

Noma pudendi is a form of gangrene that occurs spontaneously in debilitated children; it resembles noma of the face. Is very rare.

Tuberculosis, in the form of lupus, is sometimes encountered. Occurs as irregular ulcers, with necrotic bases and elevated edges.

Syphilis, usually in the form of a chancre, occurs on the vulva. Ulcers of various forms may be present, and mucous patches are very common.

Chancroid is quite frequent; is accompanied by extensive ulceration and, at times, inguinal buboes.

Elephantiasis may involve one or both labia, and cause a tremendous increase in the size of the part.

Tumors.—*Fibroma* and *fibromyoma* are occasionally found projecting from a labium or the clitoris, as polypoid tumors. *Lipoma,* as a polyp from the labium majus, is not uncommon. *Sarcoma* is rare. The *caruncle* is a small papillary growth projecting from the urethra, is very vascular, and extremely sensitive. *Papillomata* are quite common, and occur as hard, flat, or projecting masses; are present in syphilis. *Cancer* is rare, but may arise from the skin, the labium majus, or from the glands of Bartholin. Usually occurs as a squamous epithelioma, which commonly undergoes marked degeneration and ulceration. It extends in all directions, and secondarily affects the inguinal glands.

DISEASES OF THE MAMMARY GLAND

Malformations.—As an associated condition with imperfect development of the chest-walls one or both glands may be absent. They may be hypoplastic, when there is also an incomplete development of the sexual organs. A breast may be normal in other respects, but be lacking a nipple, or there may be several nipples. Supernumerary mammæ—*poly-*

mastia—may be present in both sexes, usually on the anterior surface of the chest and abdomen. They may occur on the back or thigh, and occasionally may functionate, although they are usually ill developed and lack a nipple.

Circulatory Disturbances.—*Hyperemia* is present during menstruation, during pregnancy, and at the beginning of lactation. The gland will be reddened, swollen, and sometimes painful. This congestion may also be brought about by some diseased condition of the uterus, the relationship of these two organs being very close.

Hemorrhage is due to some injury of the gland. The bleeding may take place within the connective tissue, into the glandular structures, or deeper down, behind the gland upon the muscle. The blood may escape from the nipple, it may be absorbed, or it may become encapsulated by a wall of fibrous tissue and form a hematoma. Hemorrhage may also be the result of bleeding from the ulcerated surfaces of new-growths.

Inflammation of the mammæ, or *mastitis*, may rarely be due to injury, but it is most commonly the result of infection occurring during the puerperium. The micro-organisms most frequently gain entrance through fissures of the nipple during suckling. Infection directly into the milk-ducts is not common. Mastitis may result from the extension of inflammations of neighboring structures, as caries of a rib, erysipelas of the skin, or in puerperal infection the micro-organisms may have been brought to the gland through the blood-vessels. The disease may be diffuse or involve a portion only of the gland, the latter being the more common. In the diffuse form the inflammation may extend to neighboring structures, setting up a *paramastitis*. In the circumscribed variety there is abscess formation, which may be single or multiple. The pus may escape into the milk-ducts and out through the nipple; it may be interstitial or rupture externally, in the latter case frequently causing a fistula. If the pus burrows into the deeper tissues, it may perforate into the pleural cavity and cause a fatal empyema. Occasionally the pus may be encapsulated, inspissated, and calcified. Sometimes a con-

dition of the mammæ similar to that of chronic interstitial inflammation of the organs occurs. The glands are firm and hard, due to the connective-tissue formation, and small cystic dilatations of obstructed milk-ducts may be present.

Tuberculosis of the mammary glands is rare, except as a secondary involvement in tuberculosis of the axillary nodes or other tissues. The tubercle bacilli are probably carried by the blood. Tubercles are formed which undergo caseation, and the contents escape into the acini. In this way great numbers of the bacilli can gain entrance into the milk.

Syphilis of the mammæ is very rare, but has been seen as gummata, which in healing form a dense, stellate scar.

Atrophy of the glands occurs after the menopause or when the ovaries have been removed.

Hypertrophy at the time of puberty may continue beyond the normal limits and cause an enormous development of both the glandular and connective-tissue elements of either or both breasts. If lactation takes place, the amount of milk secreted may be very great. The gland may be much enlarged, on account of a diffuse fatty infiltration or *lipomatosis*.

Tumors.—*Sarcoma* is rather infrequent, is usually of the round-cell variety, and may be diffuse or in circumscribed nodules. One gland alone is generally involved. In the diffuse form the mamma rapidly enlarges, the growth infiltrates in all directions, the skin soon becomes firmly attached and may ulcerate. The structure of the tumor differs in different parts. It may be quite cystic on account of obstruction to the milk-ducts; part may be myxomatous or resemble connective-tissue. The sarcoma cells may extend into the cystic dilatations as polypoid projections—*intracanalicular sarcoma*.

Occasionally the tumors may be circumscribed. They most commonly originate within the adventitia of the milk-ducts and nipple, but may arise from any part of the connective-tissue of the gland. These tumors give metastasis by means of the blood, but they are much less malignant than the carcinomata.

Fibroma as a pure connective-tissue tumor is unusual. It

is commonly found in connection with a hyperplasia of the glandular structures.

Adenoma in a typical form is rare, is generally associated with an overgrowth of connective-tissue, and is called either *adenofibroma* or *fibro-adenoma.* According to the relation of the glandular and fibrous elements these tumors can be classified into three divisions:

"*Intercanalicular fibro-adenoma,* in which the tumor is chiefly fibrous in structure, with the ducts and acini irregularly distributed through it.

"*Pericanalicular fibro-adenoma,* in which the fibrous tissue makes distinct concentric investments of the ducts and groups of acini.

"*Intracanalicular fibro-adenoma,* in which polypoid or papillary growths extend into the ducts."

These tumors are more or less completely encapsulated, and although of the benign type, they not infrequently take on a carcinomatous growth.

Carcinoma is an extremely common tumor of the mammary gland in women between the ages of forty and fifty. About 2 per cent. of cases occur in males. The growth usually involves one breast only, and that the right more frequently than the left. It develops either from the tubules or the acini of the glands, and may start as a carcinoma or result from a malignant degeneration of a fibro-adenoma. When the growth begins in the acini, it resembles quite closely the ordinary racemose character of the gland—is alveolar in form. If it is of the tubular type, there are long tubular collections of cells.

Although at first the growth may quite closely resemble a simple adenoma, proliferative changes soon occur in the epithelium. The cells, instead of forming a single layer, increase in number and lose their resemblance to the normal structure. These new-formed cells may completely fill the acini, or they may be found within the surrounding tissue as a result of destruction of the basement membrane.

According to the relationship between stroma and parenchyma mammary carcinoma may be divided into three classes:

Carcinoma simplex, in which there is, relatively speaking,

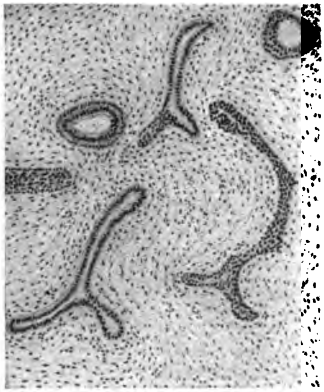

FIG. 161.

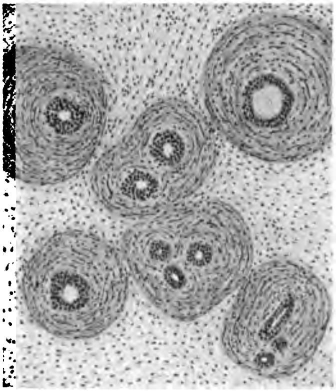

FIG. 162.

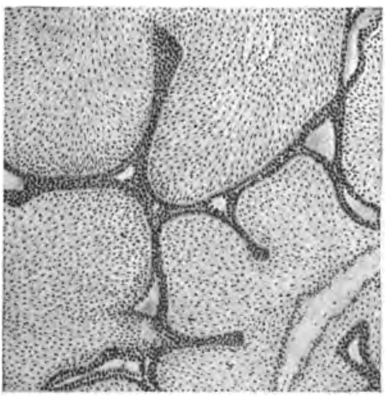

FIG. 163.

Fig. 161, Intercanalicular adenofibroma of mamma. The fibro-connective tissue bears no definite relation to the glandular canals. Fig. 162, Pericanalicular adenofibroma of mamma. The fibro-connective tissue shows a peculiar concentric relation to the glandular canals. Fig. 163, Intracanalicular adenofibroma of mamma. Papillary connective-tissue growths project into the glandular canals (McFarland).

an equal amount of connective-tissue and epithelial cells.

Is less malignant than the medullary, but more so than the scirrhous.

Encephaloid or medullary carcinoma, which is very rich in cells and poor in stroma, is soft, contains much "cancer juice," and hemorrhages are not uncommon. It grows rapidly, soon ulcerates, and is rapidly fatal.

Scirrhous carcinoma is characterized by a great preponderance of connective tissue, is hard, is slow in growth, does not tend to give metastases, and is slowly fatal. In this form there is frequently a retraction of the nipple.

The so-called *colloid* carcinoma of the breast is generally one in which a myxomatous degeneration of the connective tissue has given rise to the appearance.

Extension of carcinoma may take place directly to the skin or, by penetrating deeply, enter the chest-walls and pleuræ. Metastasis is common, takes place early, and may be very extensive, the axillary nodes being first involved. Secondary growths may also occur in distant parts of the body.

Paget's disease begins as a chronic eczema of the nipple and adjacent skin. It may have existed for ten or fifteen years with more or less complete destruction of the nipple, and then take on a carcinomatous change.

Cysts are quite commonly found, particularly in new-growths in which there has been an attempt at secretion without any outlet. Small milk-cysts may result from obstruction to the ducts. The contents of the cysts may be milky, or, through absorption of the liquid portion, become thick and caseous.

CHAPTER XXIV

DISEASES OF THE MOTOR SYSTEM

BONES

Circulatory Disturbances.—*Hyperemia* is usually associated with inflammatory disturbances of adjacent tissues. The periosteum is reddened and swollen, and the marrow is bluish-red in color.

Thrombosis may occur in the nutrient blood-vessels as a result of fracture or disease, but seldom causes any disturbances on account of the rich anastomoses. *Embolism* may occur, but seldom causes trouble.

Hemorrhage takes place as a result of injury to the periosteum or the bone itself, as in fracture. Is generally soon absorbed, but if it becomes infected, suppuration may follow. Necrosis may at times be caused by the blood dissecting the periosteum away from the bone.

Rachitis.—*Rickets* is a constitutional disorder in which there are nutritional disturbances involving, to a greater or lesser extent, all the bones of the skeleton. The long bones become shortened, thickened, and twisted, and there is a lack of calcium salts. It makes its appearance most frequently in the first or second years of life, but may be delayed until several years later. The cause is not known, but it evidently depends upon poor hygiene and malnutrition, consequently it is more common among the poorer classes.

The head has a peculiar square shape and is large in proportion to the body. In infants the anterior fontanel may persist for three or four years, and the bones of the skull may contain localized areas in which there is a lack of mineral salts—*craniotabes*. The chest is usually prominent, coming to a distinct angle—"pigeon-breast"—and the anterior ends of the ribs at the junction with the cartilage are distinctly

enlarged, forming the *rachitic rosary*. If the disease is severe, there may be involvement of the spinal column. If the curvature is forward, *lordosis;* if backward, *kyphosis;* sideways, *scoliosis*. These curvatures may occur in combination. The pelvis may show changes that have a direct influence upon childbirth; it is distinctly flattened. The anteroposterior diameter is decreased, while the transverse is increased. The tibiæ and fibulæ are usually much curved outwardly, the femur anteriorly. The lesions are most marked at the extremities of the long bones. Microscopically there is seen at the extremities an irregular bone-formation with a deficiency of lime salts in many areas, while neighboring portions will show ossification. The normal laminated appearance is absent.

The marrow is of the red variety, similar to that in the fetus, being rich in cells. The increase in size of the heads of the long bones is due to an increase of the cartilage cells and enlarged marrow-spaces. Associated with the lesions of the bones are gastro-intestinal disorders and fibrous hyperplasia in both spleen and liver. There are a decrease in the erythrocytes and an increase in the leukocytes.

Osteomalacia is a condition of softening and flexibility of the bone following absorption of the bone salts. It is most common in women of the poorer classes, and frequently appears in connection with pregnancy. It is more common in certain regions—along the Rhine and in central Germany—than elsewhere. As a result of the flexibility of the bones, fractures are very common and all varieties of deformities may appear. The pelvis is often the seat of a typical deformity. As a result of the pressure of the spinal column from above and from the femurs below, the pubes are pushed upward and forward like a beak, the sides of the pelvis inward, and the iliac crests outward. From above, the opening in such a pelvis is triangular. Microscopically it is seen that the loss of bone salts takes place first at the periphery and extends toward the center. The laminated condition remains unchanged until late in the disease, and the marrow is red. Where the bones are much bent or there has been a fracture, the regular histo-

logic structure is not retained. The bones are soft and easily broken or cut. Cachexia appears eventually, and the patient usually dies from exhaustion following repeated fractures or from some intercurrent disease.

Atrophy of the bones occurs constantly, but regeneration continues also. In various conditions the destruction is too rapid and actual atrophy takes place—either general or local. Local atrophy is usually the result of pressure causing obstruction of the periosteal blood-vessels, thus interfering with the nutrition of the bone. When the bones become very brittle as a result of atrophy, the condition is known as *fragilitas ossium.*

Hypertrophy may be general or local, the latter being due to increased work brought upon certain areas of muscular attachment. General enlargement seems to be due to various nerve disturbances, and is frequently associated with lesions of the pituitary body, as in a akromegaly.

Inflammation may involve the covering of the bone,—*periostitis,*—the bone itself,—*ostitis,*—or the marrow—*osteomyelitis.* It is due to traumatism and infection.

Periostitis may be acute or chronic. In the *simple* or *acute* form the periosteum becomes swollen, hyperemic, and infiltrated with blood. The process may stop there, but if infection has taken place, there is generally the formation of an abscess beneath the periosteum. In such a case the nutrition of the bone is interfered with, and the osseous tissue begins to undergo destruction—*necrosis.* Large portions may separate and be discharged as *sequestra* through a superficial opening. The process may extend into and involve the marrow cavity, and death may result from septicemia or pyemia. The so-called *malignant periostitis* is merely a very severe purulent periostitis of considerable extent, and accompanied by marked destruction of the bone.

Chronic periostitis may have originated as such, or it may have followed an acute form. It may be *fibrous,* in which the periosteum becomes very greatly thickened and adheres very closely to the bone. *Ossifying periostitis* is a condition in which there is the formation of loose bony tissue beneath the

periosteum. It is found in pregnancy, in tumors, and in syphilis and tuberculosis of the bones.

Bony excrescences, as exostoses and osteophytes, may form and the surrounding connective tissue may become involved—*parostitis.*

Osteitis and osteomyelitis have to be considered together, as the two conditions do not exist separately. This condition results from infection, either by micro-organisms from the blood, from local infections, or from a pre-existing periostitis. The inflammation generally starts in the medullary cavity of the long bones, the marrow of which is much congested at first and dark red in color. Later there is a cellular infiltration, and finally suppuration occurs, the pus being localized or in streaks. The surrounding bone becomes involved, and more or less extensive necrosis follows. The periosteum becomes inflamed, and the suppuration may extend to and involve the epiphyses. The necrotic portion may remain as a sequestrum, being surrounded by a layer of normal bone. As long as the sequestrum remains, healing will not take place, but when it is removed, either entire or by absorption, new bone is formed and there is a return to nearly the normal. When the condition terminates fatally, it is generally due to pyemia.

Chronic osteomyelitis generally is a condition following the acute form as a result of a retained sequestrum. The changes in this disease are more marked in the bone than in the marrow. There are two varieties of the chronic form: *osteoporosis*, in which absorption takes place with an increase in the size of the Haversian spaces. The bone becomes more spongy, and the enlarged spaces become filled with marrow; *osteosclerosis*, in which there is an increased formation of bone, particularly beneath the periosteum, but also within the marrow cavity. The subperiosteal deposit may be very dense and possess an ivory-like eburnation.

Necrosis refers to the destruction of large portions of bone, as a result of interference with the blood-supply or from the extension of disease from the periosteum or neighboring bone.

The dead piece remains as a *sequestrum;* part having been absorbed, the rest remains in a cavity surrounded by granula-

tion tissue and pus. It acts as a foreign body, and constantly keeps up a suppurative reaction in the adjacent structures. A fistulous opening or *cloaca*, communicating with the exterior, generally forms, and the pus continues to discharge through it. This may continue for years if the sequestrum is so large that it cannot pass through the opening. When it does escape or become absorbed, healing takes place. *Phosphorous necrosis* of the maxillæ is frequently observed in those who are employed in the manufacture of phosphorous matches. The process begins as a thickening of the periosteum, with suppuration, caries, and necrosis, which may be very widespread and destructive. The condition is favored by the presence of carious teeth.

Tuberculosis of the bones is most frequent in childhood and may begin during uterine life. The epiphyses of the long bones are most commonly involved, then the spinal column, the wrist- and the ankle-joints. The infection may be hematogenous from tuberculosis of other organs, or it may result from direct extension by contiguity. The disease may occur in a miliary form within the bone-marrow, or as a localized condition of the periosteum. The process extends more rapidly in the spongy bone and frequently involves the joints.

In the marrow cavities of the bone tubercles appear as small grayish areas surrounded by a zone of active hyperemia. These extend through the Haversian canals, involving compact as well as spongy layers. These areas undergo caseation and are accompanied by caries of the bones. The degenerated masses may so obstruct the blood-supply as to cause necrosis. As the bone is destroyed, broken-down masses are formed, and these may escape into the surrounding tissue, giving rise to a cold abscess. There is little inflammatory reaction; the degenerated tissue follows along the lines of least resistance, along muscle-sheaths, and may finally be evacuated at some distance from the seat of the disease. This is particularly common in Pott's disease, tubercular caries of the spine. Occasionally encapsulation and absorption take place, but this is unusual. The periosteum surrounding the degenerated area may undergo a marked new bone-formation.

Very extensive deformities may ensue in this disease, either as a result of destruction of the bone or from the formation of osteopyhtes.

In long-continued tubercular degeneration of the bone extensive amyloid changes in the internal organs are common.

Syphilis of the bones may be either hereditary or acquired.

In congenital or hereditary syphilis the epiphyseal function is marked by a narrow whitish or reddish-white line extending through the bone. The cartilage at this point is much thickened, and the calcified portions project irregularly into the marrow cavity. As the condition progresses the cartilage may become almost gelatinous, and finally there may form a distinct, irregular, yellowish line of granulation tissue separating the diaphysis and the cartilage. This is one of the characteristic signs of congenital syphilis.

Acquired syphilis generally involves the periosteum and occurs usually in the tertiary stage. It may appear as a periostitis of the skull, tibia, ulna, etc., with thickening due to hyperplasia. This may become gummatous, set up a superficial erosion and necrosis of adjacent bones, with quite extensive loss of tissue. This is not infrequent in the skull.

Leprosy generally begins in the marrow in the form of nodules, and sets up an osteomyelitis. In one form, *lepra mutilans*, there may be marked destruction and absorption of the phalanges.

Actinomycosis gives rise to an osteomyelitis with more or less caries and necrosis.

Tumors.—The periosteum may be the seat of a *fibroma*, a *myxoma*, or a *lipoma*. *Chondromata* also develop from the periosteum, are most common on the extremities, and are generally multiple. The *osteomata* are tumors formed of bone.

Sarcoma is the most frequent and the most important bone tumor, being also the only primary malignant growth. Any of the various forms may occur, the spindle-cell and the giant-cell being the most common, but round-cell, pigmented, and angiosarcoma are occasionally seen. The tumor may originate from the periosteum, the bone-marrow, or the

bone. The giant-cell sarcoma, or epulis, is found upon the lower jaw, is usually only slightly malignant; may last for years and not give metastases. When the growth originates within the medulla, the bone gradually becomes much thinned and may break, allowing the tumor-cells to escape. An *osteoid* sarcoma is one generally arising from the periosteum at the ends of the long bones, and is characterized by the formation within it of irregular masses of bone.

Secondary infection may give rise to a general sarcomatosis of the bony structures.

Chloroma is a form of sarcoma that is green or yellow in color, and is usually found in parts of the skull.

Carcinoma probably never occurs except as a secondary involvement, particularly in cases of carcinoma of the breast, thyroid gland, and prostate.

Fractures.—A fracture is a solution in the continuity of a bone, and is usually due to traumatism or to muscular contraction. The break may occur in any direction in the bone—transverse, oblique, or parallel to the long axis, or any modification. If the break is not complete of all fibers, it is known as a *green-stick* fracture; this is common in children. If there are several fragments it is called a *comminuted fracture.* If an opening to the surface is made, it is a *compound fracture.*

When a bone is broken, reparative processes take place and the bone is regenerated. After the fracture there is an extravasation of blood between the fragments. Proliferation of the cells of the periosteum occur, and calcareous matter is deposited, forming cartilage, or *callus.* This is slowly converted into bony tissue. At first there is an excess of it, but all except that immediately surrounding the fracture is absorbed. The callus is derived from the periosteum and from the medullary cavity. At the time of its formation new blood-vessels appear to assist in the nutrition. More or less deformity may accompany the process of repair, according to whether or not the broken fragments were carefully approximated.

DISEASES OF THE JOINTS

Luxation is a condition in which the articulating surfaces are disturbed in their relations. It is due to traumatism, and when it occurs, there is generally a rupture of some of the ligaments with laceration of the adjacent soft parts. If the surfaces are restored to their normal position, inflammatory reaction takes place, the capsule and the ligaments heal, and a normal condition supervenes. If restoration has been incomplete or only partial, absorption of the end of the bone occurs, the periosteum undergoes calcification, and a new joint may be formed. Fibrous tissue, cartilage, or bone may, however, form, and bind the joint so closely that no motion is preserved; this condition is called *ankylosis.*

Hyperemia of the joints is found after injuries, in mild inflammations, and in rheumatic conditions. The synovial membranes are mainly affected. They are pinkish, swollen, and the synovial fluid is both increased in amount and more watery than normal.

Hemorrhage generally follows an injury, but may occur in inflammations and in the course of hemorrhagic diseases. It is called *hemarthrosis.* If infection does not occur, absorption slowly takes place, leaving the tissues considerably pigmented.

Arthritis, or inflammation of a joint, may be due to an injury or to a hematogenous infection in certain diseases, as scarlet fever, pyemia, or gonorrhea. The synovial membranes are chiefly involved, the cartilages less so and secondarily. If all the structures of the joints are involved, it is a *panarthritis.* The exudation into the joint may be serous, fibrinous, or purulent, and the after-results depend mainly upon which variety of arthritis existed. If *serous*, the fluid is generally soon absorbed and the joint returns to a normal condition. If, however, there is a *serofibrinous* exudation, the process will probably continue longer and adhesions form within the joint. The most serious variety is the *purulent.* The entire joint is frequently attacked, the synovial membrane swollen and hyperemic, and the surface covered by pus-

cells and fibrin. The joint contains a greater or less amount of pus, and the articulating cartilages may be eroded and even necrotic, with involvement of the neighboring bone.

Any of the above varieties may become chronic, and in the serous form a *hydrarthrosis*, or collection of fluid in the joint, may be present. In the purulent variety, as a result of the destruction of cartilage or bone, the joint may lose all power of motion—ankylosis—from the formation of fibrous and bony adhesions.

Acute articular rheumatism is a condition in which one or more joints are acutely inflamed and painful. This process is generally considered to be the result of infection; staphylococci, gonococci, and other organisms have been recovered from the affected joints. The joints are swollen, red, and painful, and the surfaces are covered more or less by masses of fibrin, some of which may be suspended in the exudate. There are seldom many leukocytes present. As a result of the inflammation, either fibrous or bony ankylosis generally occurs, with more or less subsequent deformity.

Arthritis deformans, or rheumatoid arthritis, is a chronic process occurring, as a rule, in people past middle life. There is a proliferation of cartilage cells, and finally softening, with ulceration of the superficial cells. This gradually extends down to the bone, the surface of which frequently shows some absorption. At the edge of the joint exostoses may form. The ligaments become contracted and fibrous, and ankylosis occurs. As a result of the destruction of bone and formation of connective tissue, all varieties of subluxations (partial dislocation) and deformities occur.

The joints most commonly involved are those of the hip and knee, metacarpo-phalangeal articulations of the hand, and the corresponding ones of the feet.

Senile arthritis resembles very closely the former variety, except that it is more widespread, involving the hip, shoulder, and elbow, and occurs in old people.

Neuropathic arthritis occurs in spinal diseases, particularly posterior sclerosis, syringomyelia, and transverse myelitis. The joints of the lower extremities are more commonly

involved. The lesions closely resemble those of arthritis deformans, but there is seldom much pain.

Arthritis uratica, or **gout,** is a condition in which there are deposits of urates within the joints and the adjacent connective tissues. It generally affects the smaller joints of the hands and feet, particularly the metatarso-phalangeal articulation of the great toe. The joint becomes red, swollen, and very painful; there is a serous effusion into it, and the salts are precipitated from this fluid. These substances may form quite large, chalky deposits. After repeated attacks chronic changes may occur within the joint, such as softening and erosions of the cartilage, hyperplasia of the periosteum, with some ossification. Besides the local conditions, there are constitutional disturbances and also widespread tissue changes, particularly atheroma of the blood-vessels.

Tuberculosis of the joints is most common in childhood, and may be primary or secondary. It occurs most frequently in the hip, knee, and spine, although any joint may be attacked. In the primary form the synovial membranes are first involved. The secondary variety generally results from extension from tuberculosis of the bone.

In the synovial membrane are found extensive soft granulations in which are seen small yellowish or gray tubercles. Caseous degeneration appears early, as a rule, and the joint may be filled with broken-down tissue forming a cold abscess. When the process has extended from the bone, there is marked destruction of tissue around as well as within the joint. The abscess contents may burrow, and emptying upon the surface form a sinus.

Death may result from associated amyloid disease or exhaustion.

If the process subsides, the joint is usually ankylosed in an abnormal position.

Syphilis of the joints is found in children as a congenital lesion. There are thickenings of the ligaments, ulceration of the cartilages, and a purulent exudation. Occasionally gummata may be present. In adults, as a result of acquired syphilis, there may be a serous or sero-fibrinous inflamma-

tion of the joint. Gummata sometimes occur, and as a result of degeneration with fibrous formation may cause lesions similar to arthritis deformans.

Tumors.—The synovial fringes may show small lipomata and fibromata. These may become separated and lie free within the joint, the so-called "rice bodies," which are small structures originating from the villi of the synovial membrane; are generally quite numerous, thirty or forty being found at times. The joints may be secondarily involved by new-growths in adjacent tissues.

DISEASES OF THE TENDONS AND BURSÆ

Tenosynovitis refers to an inflammation of the sheath of a tendon and may be acute or chronic, or serous, fibrinous, or purulent, or any combination, according to the exudate. The purulent is usually the result of a secondary infection.

Bursitis, inflammation of the bursa, is usually found in the prepatellar bursa as a result of chronic irritation, and is accompanied by effusion.

Tuberculosis may involve either of the above structures secondarily to disease of the bones and joints.

DISEASES OF THE VOLUNTARY MUSCLES

Circulatory Disturbances.—*Anemia* may be part of a general condition or the result of local interference. Degenerations of the muscle occur if the anemia has been sufficiently severe or long continued.

Hyperemia occurs during exercise and in inflammatory processes.

Hemorrhage results from injuries or from the rupture of a blood-vessel that is either diseased or in which the blood-pressure has been too great.

Degenerations.—*Necrosis* of muscle-fibers may follow injuries, burns, and various local causes; the tissue becoming blackish in color and disappearing.

Cloudy swelling is found in infectious and toxic conditions in general and in the neighborhood of inflammatory changes and tumors. The sarcoplasm becomes very granular and

the striations disappear. Fatty degeneration frequently follows.

Fatty metamorphosis follows the cloudy swelling when the original cause has been very harmful, as in phosphorous and arsenic poisoning. The muscles are flabby and yellowish in color. The fibers lose their striations and become filled with fat-drops.

Fatty infiltration consists of the deposit of fat between the muscle-fibers. It is most typical in pseudo-hypertrophic muscular atrophy, but may be present to some extent in obesity.

Amyloid degeneration is rare in voluntary muscles, but occurs occasionally in the non-striated.

Calcification occurs in the form of ossifying myositis.

Hyaline Degeneration.—In this the muscle-fibers become granular and cloudy, and the transverse striations are obscured. The hyaline change appears in streaks, the fibers having become transformed into a homogeneous mass within the sarcolemma. The fibers break in two, and rupture of the muscle may occur. This degeneration is found in the course of infectious conditions, as typhoid fever and smallpox. It is found usually in the rectus abdominis, in the long muscles of the thigh, in the diaphragm, and in the heart.

Atrophy.—Simple atrophy is usually either senile or the result of inaction. The fibers become smaller, and there is usually some hyperplasia of the connective tissue. *Brown atrophy* is quite common as a senile change. In it brown pigment particles are deposited in the muscle-fibers near the nuclei, and impart a brown color to the tissue.

Progressive muscular atrophy usually involves the muscles of the hands, arms, and shoulders, but may attack those of the diaphragm and back. The muscles are pale and flabby, and show various degenerations, such as transverse division, longitudinal separation, coagulation necrosis, and vacuolation. At the same time there is a connective-tissue hyperplasia.

Pseudohypertrophic muscular atrophy commonly makes its appearance in the muscles of the calf, thigh, and upper extremities. The muscles are much larger than nor-

mal, but are soft and flabby. Microscopically there is seen a great hypertrophy of the intermuscular connective tissue, with fatty infiltration and atrophy of the fibers.

Many of the muscular atrophies depend upon various obscure nerve lesions, as such changes are found in syringomyelia; acute anterior poliomyelitis; lateral scleroses; in degenerations of the peripheral nerves; in diseases of the anterior nerve-roots; in diseases of the pons, and possibly of the nerve-endings.

Inflammation or **myositis** is generally the result of inflammatory changes in adjacent tissues. It may be acute or chronic, local or disseminated.

The process is usually not severe; the muscle is swollen, reddened, and there is a slight exudation, as well as a round-cell infiltration. Some of the fibers may degenerate.

Hemorrhagic myositis is characterized by marked hemorrhagic infiltration into the muscle. It may follow extension from gangrenous processes near by.

Purulent myositis is characterized by local or disseminated abscess formations, with necroses and breaking-down of the tissues. It is due to infection by micro-organisms as a result of traumatism through conveyance by the blood or lymphatics or to infectious emboli. In the healing, masses of connective tissue may form and occasion more or less severe deformities, due to shortening. Sometimes an abscess may become encapsulated and calcified.

Acute disseminated polymyositis is a condition in which many muscles are simultaneously affected. It is of infectious origin. There is round-cell infiltration between the fibers, many of which show degenerative changes.

Chronic myositis may be a slow process, found in tuberculosis and actinomycosis, in which there is long-continued suppuration without fibrosis. The ordinary form is the *myositis fibrosa*, in which there is a slow increase in the amount of connective tissue with degeneration and atrophy of the muscle-fibers. It follows acute myositis and sometimes after certain nerve-lesions.

Myositis ossificans is a chronic inflammatory condition in

which there is actual bone-formation within the intermuscular connective tissue, in fascia, and tendons. It is found in the deltoid, pectoral, and adductor muscles, and appears to be the result of long-continued and repeated slight injuries.

Myositis ossificans progressiva is a peculiar condition beginning in the muscles of the back of the neck. The ossifying process gradually extends to other muscles of the trunk. The deposit of bone may become very great and cause marked interference with muscular contraction.

Tuberculosis of the muscle is commonly secondary to lesions in adjacent tissue, and appears either in the form of caseous degeneration, cold abscess, or of fibrous formation. Hematogenic infection is uncommon in general miliary tuberculosis, but may occur.

Syphilis is rare, but may be found in the form of gummata, or as a diffuse hyperplasia of the muscular septa, with atrophy of the muscle-fibers. The muscles usually involved are the biceps, masseter, tongue, and back.

Glanders and **actinomycosis** may involve the muscles by extension.

Tumors, as a rule, originate within the intermuscular connective tissue and may be any one of that type—lipoma, fibroma, etc. The *sarcoma* is not infrequent in any of its combinations, and may be spindle- or round-celled in type. *Carcinoma* is always secondary, and is found in the neighborhood of similar growths in the mammæ, stomach, skin, etc., as a diffuse infiltration.

Parasites are not uncommon, the most frequent being the *Trichina spiralis*, the *Cysticercus cellulosæ*, and the *Tænia echinococcus*.

CHAPTER XXV

THE DUCTLESS GLANDS

THE THYROID

Malformation.—It may be congenitally absent, variations in size are common, and small accessory glands may occur. Total absence is usually associated with cretinism or idiocy.

Atrophy takes place normally in old age.

Hypertrophy, or *goitre*, is a condition in which there is hyperplasia of the interstitial and glandular tissues. These enlargements are classified under various headings.

Graves' or *Basedow's* disease, *exophthalmic goitre*, is an enlargement of the gland associated with certain cardiac and eye symptoms. The blood-vessels are dilated, interstitial hemorrhages may occur, and these are sometimes followed by necrosis. There is a proliferation of the epithelium of the acini with a decrease of the colloid material. The symptoms may be due to an excess of iodin formation.

Parenchymatous goitre consists of an accumulation of secretion within the acini which have undergone hyperplasia. The enlargement may be uniform or nodular.

Cystic goitre is a variety of the above in which the walls separating the acini have atrophied and allowed large accumulations of colloid material to form (Fig. 10).

Fibrous goitre is one in which there has been a great increase in the connective tissue. The growth is slow, and the resulting tumor is very hard, dense, and at times calcified. Hyaline degeneration of the connective tissue and blood-vessels frequently occurs.

Adenomatous goitre is one in which there has been a distinct increase in the number of the alveoli. It resembles an adenoma except that the growth is not circumscribed.

The effects of goitre may be *local*, as a result of the pressure exerted, or *distant*, on account of some disturbance of nutrition. Its cause is unknown. In certain countries it is endemic, and more common in high altitudes than in low.

It is very commonly associated with cretinism, occurring in about 60 per cent. of such cases.

Hyperemia occurs in cardiac disease and when there is obstruction to the circulation by tumors. In Graves' disease the gland is very vascular.

Inflammation (thyroiditis) is not common. It may follow traumatism or infection, and varies in its severity. Suppuration may occur with, at times, fatal results. The pus may remain confined within the capsule, and by pressure interfere with respiration. The abscess may perforate the trachea, esophagus, or skin, or it may follow along the cervical fascia into the mediastinum.

Tuberculosis, syphilis, and **actinomycosis** are very unusual, but have been observed.

Tumors.—*Fibromata* in the form of circumscribed nodules occasionally occur.

Sarcoma is a common primary tumor of the gland. It occurs in all forms, the round-cell variety being the commonest.

Carcinoma is the commonest form of primary tumor. It begins usually in an adenomatous goitre, and is of the adenocarcinomatous type. It grows rapidly, soon invades the tissues of the neck, and frequently gives metastases. Degenerative changes are quite common.

Adenoma can seldom be differentiated from a glandular hyperplasia unless the growth is distinctly circumscribed.

THE ADRENALS

Malformation.—They are seldom absent, but may be unusually small. Supplementary adrenals are not uncommon, and inclosure of fragments in the liver, kidney, and genital organs is quite frequent. These may give rise to *hypernephromata*.

Fatty degeneration is quite common. The gland is

yellowish and soft. The medullary portion mainly is involved, the cortex remaining as a thin wall. On account of post-mortem changes taking place so rapidly, it is at times very difficult to accurately judge the importance of the lesion.

Amyloid changes occur in the blood-vessels as a part of general amyloid disease.

Pigmentation is present in senility. The cortex contains fine yellowish granules.

Hemorrhage sometimes occurs either as a result of injury or of constitutional conditions. The blood may be absorbed or encysted, with induration and calcification.

Syphilis occasionally occurs, either as a gumma or an induration.

Tuberculosis of the adrenals is not uncommon. It is frequently a part of a general miliary involvement.

Primary tuberculosis, in the form of a caseous degeneration, is the lesion most generally associated with Addison's disease. The adrenals are enlarged, nodular, and the capsule is thickened. Caseous areas and small cavities filled with a thick, curdy pus are frequently found. Calcification may take place.

Tumors.—*Sarcoma*, *adenoma*, and *carcinoma* may occur as primary growths, and are not infrequently associated with Addison's disease. As secondary growths they are more common.

THE SPLEEN

Malformations.—Total absence may occur. It may be divided into lobes, and accessory or supernumerary spleens of small size are quite common.

The organ may be unusually movable. It may be much displaced by pressure from neighboring organs or collections of fluids.

Anemia may be part of a general condition or follow severe hemorrhage. The organ is smaller than normal, pale, and the capsule is much wrinkled. On section, the stroma is prominent and the color is a reddish-gray or slate.

Hyperemia.—*Active hyperemia* is physiologic after a

large meal, and is almost constantly present in the infectious fevers. The spleen may be several times its normal size, is dark red in color, and the capsule is greatly stretched and the pulp so very soft, almost semifluid, that it oozes from the cut surface. If the condition is acute, the swelling is due to the hyperemia. If long continued, the connective tissue may increase in both the trabeculæ and the capsule.

This active hyperemia is especially common in typhoid fever, and the micro-organisms can usually be recovered from the spleen.

Passive hyperemia is due to obstruction of the circulation, as in cirrhosis of the liver and chronic heart and lung diseases. The condition is known as cyanotic induration, on account of the characteristic color and firmness. The spleen is larger and bluish-red in color; the capsule is tense, and the pulp soft. As the condition persists, there is an increase in the connective tissue of the capsule and the trabeculæ. There may finally be an atrophy of the splenic pulp, with contraction of the fibrous tissue, so that the organ becomes smaller, firmer, and somewhat distorted.

Hemorrhage is usually the result of traumatism, and occurs beneath the capsule. A common form is that which occurs in *hemorrhagic infarction* as a consequence of embolism. The conic area has its base toward the periphery and the apex toward the hilum. It rapidly breaks down, and if micro-organisms are present, an abscess may form. Otherwise the detritus is gradually absorbed and replaced by fibrous tissue which forms an irregular, contracted scar in which there is frequently more or less pigment.

Embolism is quite common and causes either hemorrhagic or anemic infarcts. The anemic is similar to the above, except that it is paler on account of containing less blood.

Thrombosis of the splenic vein is generally secondary to a similar condition of the portal vein.

Splenic tumor is the term applied to the enlargement that occurs in infectious diseases. The organ is large, dark colored, red or reddish-black, and very soft; the capsule is

stretched; the trabeculæ and the Malpighian bodies are invisible on section, and the tissue is very friable and mushy. Microscopically the vessels are dilated and the pulp is composed of great numbers of lymphocytes and polymorphonuclear leukocytes. Many large mononuclear cells containing erythrocytes are present. Mitotic figures are frequently found in them. Small areas of focal necrosis are also frequently present.

The enlargement of the spleen subsides as the disease declines, but it seldom gets quite as small as before the attack, on account of the fibrous overgrowth that occurs.

Acute splenitis is usually of a suppurative character, due usually to hematogenous infection. Abscesses, either single or multiple, form. They may be absorbed or may rupture into some neighboring cavity, as the peritoneal, or into the stomach, intestine, lung, or pleura.

Chronic splenitis is generally diffuse, and is characterized by a great hyperplasia of the connective tissue.

The spleen is at first enlarged, but becomes smaller as the process continues. The capsule is stretched and much thickened, and may contain circumscribed areas that are almost cartilaginous in their density. The trabeculæ are also thickened. The organ is then quite firm, and may be dark in color on account of the presence of pigment.

Tuberculosis of the spleen is rare as a primary affection, but is quite frequent as a secondary condition, and appears as a miliary infection. The tubercles are small grayish spots, not unlike the Malpighian corpuscles. They undergo a central caseation.

Syphilis is very rare, but occurs in the form of gummata. They are generally multiple, and at first grayish, later becoming yellowish on account of degeneration in the central part of the node. There may also be a diffuse increase of the connective tissue.

Atrophy of the spleen is very common in old age. The capsule is wrinkled and thickened, and the organ is pale, flabby, and pigmented, and there is an increase in the stroma. Circumscribed areas in the capsule of extreme thickness and

cartilaginous density may be present and be the cause of atrophy.

Degenerations.—*Amyloid* disease affects the spleen more frequently than any other organ. It makes its appearance in the walls of the blood-vessels in the Malpighian bodies, and involves the adjacent tissue. The bodies become enlarged, pale, and translucent, resembling boiled sago,

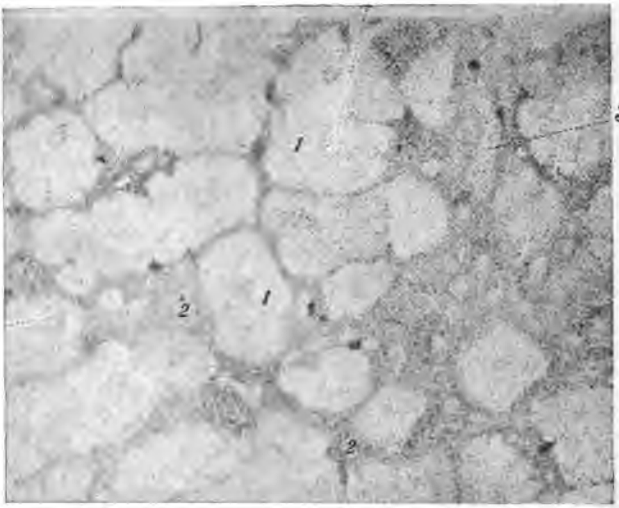

FIG. 164.—AMYLOID DEGENERATION OF THE SPLEEN (SAGO SPLEEN). × 24 (Dürck).

1, An amyloid follicle, in which are seen only a few nuclei; the blood-vessels, in transverse section, have also undergone amyloid degeneration; 2, compressed pu!p-spaces; 3, trabeculæ.

hence it is known as the *sago spleen.* Occasionally the degeneration may be more diffuse, affecting the connective-tissue stroma. The cut surface is dry, translucent, firm, and friable, and is about the same color as dried beef. The edges also are rounded. The degenerated areas give a mahogany-brown color on the addition of iodin.

Pigmentation of the spleen is found in chronic congestion,

as in cirrhosis of the liver and in malaria. Hemolysis takes place, and the freed pigment is found in the walls of the blood-vessels and in the parenchyma cells. In malaria the pigment is melanin, in other conditions hemosiderin. External pigments, as coal-dust, may lodge in the spleen. It gains entrance into a blood-vessel by erosion from pressure of an anthracotic lymph-node.

Calcification is found occasionally in old infarcts, in a thickened capsule, and in degenerated areas of tuberculosis and syphilis.

Leukemia.—The spleen becomes greatly enlarged, weighing at times as much as 5 to 10 kilograms. The capsule is much thickened. In the early stage the organ is enlarged and soft, but finally becomes firm and dense, on account of the hyperplasia of the lymphoid tissue. On section, the spleen is seen to be very much congested, and the Malpighian bodies appear quite prominent.

There is anemia resulting from pressure of the capsule on the pulp; many of the cells degenerate, and both anemic and hemorrhagic infarcts may occur. On section, the cut surface is found to be very mottled. Reddish areas, small yellowish necrotic masses, whitish bodies of lymphoid tissue, and infarctions may all be present. Microscopically the Malpighian corpuscles are found much enlarged, and contain cells showing mitoses. The new cells may be larger than normal, and giant-cells are occasionally seen. The pulp is congested and degenerated, containing pigment and large phagocytic cells in which are found erythrocytes and detritus.

Tuberculosis is not infrequently present at the same time as leukemia, and may modify the general appearances.

Pseudoleukemia.—The gross appearances are practically the same as in leukemia, but there are differences in the microscopic picture. "In the spleen and lymph-nodes there is hyperplasia of the lymphoid tissue, proliferation of endothelioid cells, formation of uninuclear and multinuclear giant-cells, thickening of the reticulum, and final overgrowth of connective tissue. Eosinophiles, though not specific, are

frequently found in great abundance. There is also an increase in the eosinophilic leukocytes and myelocytes of the bone-marrow."

Tumors.—Primary growths are rare. Secondary sarcoma and carcinoma are frequently found in generalized metastasis.

Cysts are rare. Small ones may be due to degeneration of a follicle. Large ones are occasionally found.

Parasites are also rare, but the *Pentastomum denticulatum*, the cysticercus, and the *Tænia echinococcus* have all been described, the last the most frequently.

THE LYMPH-NODES

Anemia.—The nodes are softer, shrunken, and drier than normal.

Hyperemia is characterized by an increase in size of the nodes, which are reddish in color and very moist. The change is more marked in the capsular and cortical portions than in the center. It is generally the beginning stage of inflammation.

Atrophy of the nodes occurs chiefly in old age. The lymphocytes in the medullary portion degenerate, fatty metamorphosis of the connective tissue occurs, and the nodes become smaller, hard, and dry.

Hypertrophy is usually considered among the tumors as *lymphadenoma.*

Degenerations.—*Amyloid* occurs in cases of general amyloid disease. The tissues first affected are the walls of the small blood-vessels and the connective tissue of the trabeculæ; the endothelial cells are affected later.

Hyaline changes are occasionally seen in the walls of the blood-vessels and trabeculæ.

Calcification of lymph-nodes is a not infrequent end result in necrotic lesions. There may be small scattered areas of calcareous matter or a diffuse infiltration of the node.

Pigmentation may result from the presence of internal or external substances. Hemosiderin is the commonest blood-pigment. It may form as a result of local extravasation of

blood, or it may be carried to the node by the blood from a hemorrhage in some adjacent tissue. The pigment-granules are found within the lymphocytes or in the cells of the stroma. The amount present may be very scanty, or so plentiful as to give a rusty color to the tissue.

External pigments, as in pneumonokoniosis or in tattooing, may find their way into the lymph-nodes, being carried there by leukocytes and other phagocytic cells. As a rule, the substances acting as irritants bring about a connective-tissue hyperplasia. Occasionally softening may result instead. If septic material is conveyed to the nodes, suppuration occurs.

Inflammation or **lymphadenitis** is secondary, as a rule, to the extension of inflammation from neighboring tissues. The infection is commonly of lymphogenic origin. The node becomes swollen, hyperemic, and tender. It may be dark red from hemorrhages. Microscopically the spaces are found filled with erythrocytes, leukocytes, and some fibrin.

The process may be so severe as to bring about suppuration and abscess formation. Such a condition in the superficial nodes is termed a *bubo*. If deep-lying nodes are the seat of abscess formation, serious consequences may result from perforation into some internal cavity.

If the inflammation subsides during the early stage, absorption of the exudate takes place, the leukocytes pass into the circulation or break down, and the fibrin also softens. If there has been pus-formation, absorption may not take place. The pus causes hyperplasia of the neighboring connective-tissue cells, and they form a capsule. Such abscesses may calcify. At times the necrotic masses may be entirely absorbed and be replaced by a great overgrowth of connective tissue.

Chronic lymphadenitis may follow numerous acute attacks or long-continued irritation, as in tuberculosis, syphilis, and other chronic infectious diseases. There is an increase in the connective tissue, with usually atrophy or necrosis of the lymphoid structures.

Tuberculosis of the lymph-nodes may be primary, but is much more frequently secondary to disease in a neighboring structure. The specific organism is carried to the node by the lymph-channels.

In tuberculosis of the cervical nodes the tubercle bacillus gains entrance through the tonsil without causing disease at that point. The same condition may occur in the mesenteric nodes without involvement of the intestinal mucous membrane.

The tubercular nodes are enlarged, and at first hyperemic, although later they become paler. In the substance of the node numerous miliary tubercles may be seen, or the tissue may be represented by a broken-down caseous mass in the center. The caseation may continue until the node becomes a softened, semifluid mass. The process may involve neighboring structures, and finally rupture externally, with the formation of a discharging sinus.

If the course is less acute, there may be very extensive connective-tissue hyperplasia around the disease focus, the progress being impeded in that way. Calcification may finally take place.

This variety of tuberculosis is comparatively benign. It must be remembered, however, that although a node becomes encapsulated and even calcified, it is still infectious. Though the organisms may not be recognizable microscopically, yet injection of the material into animals will usually give rise to the disease.

The microscopic appearances are the same as are found in tuberculosis in other parts of the body.

Syphilis.—In the secondary stages there is a lymphadenitis and associated with the primary lesion there may be some enlargement of the nodes. The inguinal nodes may become quite swollen, and at times suppurate. Such a condition is, however, probably due to there being a mixed infection.

The nodes are hard, and there is no tendency to soften and suppurate. Microscopically there is seen a leukocytic infiltration, with thickening of the trabeculæ and proliferation of the endothelium of the lymph-spaces. The walls of

the blood-vessels are thickened, and show round-cell infiltration.

In tertiary syphilis small gummata may form in the lymph-nodes, particularly in the lymph-sinuses. They are grayish, degenerated, and gummy, and are composed of leukocytes, lymphocytes, and other cells, all of which show fatty and hyaline degenerations.

Leprosy, glanders, and **actinomycosis** are present at times in the nodes, and show characteristic lesions.

Tumors.—*Leukemia.*—In the lymphatic form there is a general hyperplasia of the lymphatic tissues in the body. A few nodes or many may be involved, and metastatic deposits of lymphoid cells are found where normally none exist. Little change is evident; under the microscope, the enlargement is seen to result mainly from an increase of the lymph-cells without much hyperplasia of the reticulum or vessels.

The diagnosis has to be made by the changes present in the blood.

Pseudoleukemia (*Hodgkin's disease*) is a condition somewhat resembling an infectious disease, and is characterized by certain changes occurring quite generally in the lymphatic tissues. The appearances as described in the spleen (*q. v.*) are the same as occur in the lymph-nodes. The blood shows no definite changes.

Lymphoma or *lymphadenoma* refers to all enlargements of the lymph-nodes irrespective of the cause. The nodes are described as being of two varieties, the hard and the soft.

In the *hard* variety the nodes are enlarged and hard, the capsule thickened, and the trabeculæ increased. There is a great increase in the connective tissue and some hyperplasia of the lymph-cells.

In the *soft* the nodes, though enlarged, are softer and grayish. They do not suppurate. Microscopically the increase of the lymphoid tissue is the marked feature.

The enlargement of the nodes is sometimes referred to as *lymphosarcoma*, particularly when metastatic deposits of lymph-tissue are found in various organs, as the liver, kidneys, and heart.

Sarcoma may develop in a lymph-node, and, breaking through the capsule, involve adjacent tissues. Metastases occur in the internal organs without involving other lymph-nodes, and in that way is differentiated from lymphosarcoma. Microscopically the primary tumors may resemble each other so closely that they frequently cannot be told apart. Other forms than the round-cell, such as spindle-cell, occur.

Carcinoma, secondary in origin, is a very common condition of the lymph-nodes. It is found in those nodes that are nearest to the seat of the disease, and is due to the carrying of carcinomatous cells by the lymph-stream to the node.

THE THYMUS GLAND

Malformations.—The gland may be very small or completely absent. Sometimes it is so much enlarged as to cover the pericardium and the great vessels. It generally begins to atrophy by about the second year, but traces may remain until puberty or later.

Hyperemia with punctate hemorrhages is found in cases of death from asphyxia.

Inflammation is very rare, and takes the form of small abscesses. It may occur from extension of inflammations from adjoining tissues.

Tuberculosis occasionally occurs.

Syphilis occurs in the form of gummata, particularly in the new-born with congenital syphilis.

Tumors.—*Lymphoma* and *lymphosarcoma* may originate within the thymus or its remnants.

THE BONE-MARROW

The marrow is lymphoid tissue consisting of a connective-tissue reticulum in which are numerous capiliaries and venous vessels. The marrow-cells are large and round, and contain clear nuclei of vesicular character. Besides these there are many eosinophilic cells, endothelioid cells, fat cells, nucleated and non-nucleated red blood-corpuscles, giant-cells, and cells containing erythrocytes and pigment.

In early life the marrow of the long bones is reddish, but the color finally changes to yellow, on account of the increase of the fat.

Anemia.—In *pernicious anemia* the fatty tissue disappears and the marrow returns to its early condition. The color, however, is a darker red than usual. The change begins at the epiphyses, and extends toward the center of the shaft.

In *leukemia* the marrow is rather gray in color, and scattered throughout may be seen small pale areas which consist of leukocytes. These areas may be so numerous as to give an appearance of suppuration. The myelocytes in myelogenous leukemia are supposed to be formed in the bone-marrow.

In *typhoid fever* the marrow contains areas composed of many lymphoid cells, large phagocytes, and foci of necrosis. The lesions are similar to those found in the other lymphatic tissues in typhoid.

Atrophy occurs in old age and marasmic conditions. The fat is absorbed, and the number of cells decreases.

Hypertrophy is the term applied to the changes that take place in anemic conditions.

Degenerations.—*Fatty infiltration* occurs normally up to about the sixteenth year. It may be developed excessively in cases of general obesity and in conditions of ill nutrition.

Mucoid degeneration is sometimes seen.

Fatty degeneration occurs in severe infections.

Necrosis may be part of inflammatory conditions.

Pigmentation occurs in the marrow in cases of malaria, or in conditions causing hemolysis. External pigments, as anthracosis, may be deposited in the marrow by the blood.

Inflammation or **osteomyelitis** occurs in the various severe infectious diseases, as typhoid fever, smallpox, etc. The marrow becomes redder than normal, punctate hemorrhages occur, focal necroses and cellular infiltration of the blood-vessel walls are present, and also granular degeneration of the cells. At times the marrow may be distinctly purulent. The specific diseases and tumors are dealt with in the chapter on Diseases of the Bones.

CHAPTER XXVI

DISEASES OF THE BRAIN

THE DURA MATER

Hyperemia may be active as a result of injuries or disease of the skull. Passive hyperemia may follow thrombosis of the venous sinuses. Neither of the above can be well recognized postmortem, as by that time hypostasis has taken place and the blood has sought the lower levels.

Thrombosis of the sinuses is frequently secondary to extension of inflammation from adjacent bony structures, as in mastoid and middle-ear disease. It also occurs in infectious diseases, and is usually located in the superior longitudinal sinus. Cerebral softening or abscess formation with pulmonary or cardiac embolism may follow thrombosis and cause death.

Hemorrhage is commonly due to injury, and may take place on the internal or external surface of the dura. A comparatively large amount of blood may collect between the skull and the dura,—an *internal cephalhematoma,*—and give rise to serious compression symptoms. Small hemorrhages, frequently multiple, may be found in the substance of the dura after death by suffocation.

Inflammation of the Dura.—*Acute pachymeningitis* is the result of infection following injury or disease of the skull. It may be local or general, and is characterized by the presence of pus. The dura is much thickened and swollen by round-cell infiltration, and is covered by a layer of purulent material. *Hemorrhagic pachymeningitis* is found in the old, the insane, and in alcoholics, usually in the area that is supplied by the middle meningeal artery. There is an escape of erythrocytes to a greater or less extent, at times so marked

as to simulate a hemorrhage. The coloring-matter may be absorbed and leave a collection of serous fluid—a *hygroma*.

Chronic internal pachymeningitis is of obscure etiology, probably hematogenic, and is usually accompanied by disease of the pia and arachnoid. It is characterized by the deposition of numerous layers of fibrinous exudation upon the internal surface of the dura. These gradually undergo fibrous replacement, with frequently the formation of many new capillaries. The dura becomes more adherent to the bone, and calcareous infiltration is sometimes encountered.

Tuberculosis of the dura usually follows tubercular dis-

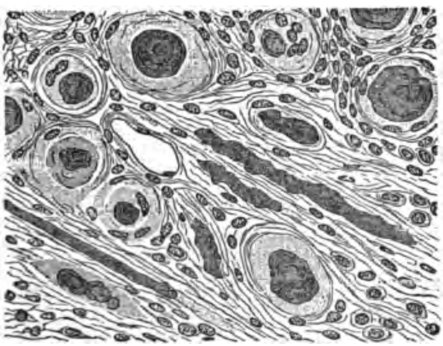

FIG. 165.—SECTION OF A PSAMMOMA OF THE DURA MATER. × 200 (Ziegler).

ease of the bones of the skull or of the pia-arachnoid. It may be present as miliary tubercles or as large caseous masses.

Syphilis may give rise to a *pachymeningitis fibrosa*, causing a dense thickening of the dura. It may also be present as gummata, which may have originated either within the dura or within the bones of the skull, and have secondarily invaded the membrane.

Tumors.—The most common is the *sarcoma*, which may be either spindle or round-celled, and quite often alveolar.

These growths extend from the inner surface of the dura toward the brain. They may be flat or more elevated, and vary greatly in size. If they form on the outer surface of the dura, they may cause absorption of the bone and perforation. If the blood-supply is very rich, these growths are called *angiosarcoma*. *Endothelioma* may develop upon the inner surface of the membrane. Other forms of primary tumors are rare, psammoma, lipoma, and fibroma seldom occurring.

Secondary tumors may follow malignant disease of neighboring structures—may be sarcoma, glioma, or carcinoma.

Parasites are rare; the echinococcus and the *Cysticercus cellulosæ* have been described.

THE PIA AND ARACHNOID

Circulatory Disturbances.—*Anemia* occurs only as a part of a general condition.

Active hyperemia is frequent, being the earliest stage of meningitis. It is also found in death from alcohol, in the infectious fevers, as typhoid and cholera, in certain poisonings, and in delirium of various kinds. The pia is red, and the smaller vessels are injected. The subarachnoid fluid may be increased in amount and cloudy.

Passive hyperemia is rather difficult to recognize postmortem, on account of the hypostasis that occurs. The large veins are distended and tortuous, the arachnoid is cloudy, and there may be more fluid than normal. This condition occurs in chronic heart and lung diseases and in venous obstructions.

Hemorrhage into the subarachnoid space from the vessels of the pia may occur in anthrax and in such diseases as scurvy, hemophilia, and in severe infections. The hemorrhages may be numerous and small, or there may be a single large collection of blood between the pia and arachnoid. This latter form is generally the result of some severe injury, or due to the rupture of an aneurysm. The blood, instead of being upon the surface of the brain, may gain entrance into the ventricles.

Small collections of blood may be absorbed and leave noth-

ing but a small, and slightly yellowish area. If the amount has been large, the pigment may be absorbed and leave a clear, serous fluid.

Edema may be present as an increase of the cerebrospinal fluid. A large collection of fluid between the pia and arachnoid is known as an *external hydrocephalus*. In senile atrophy of the brain there is an accumulation of fluid to fill out the loss of substance—*hydrops ex vacuo*. The edema may be gelatinous in character in paresis and insanity.

Inflammations.—Leptomeningitis or inflammation of the arachnoid and pia may be acute or chronic, and the acute may be classified according to the exudate.

Acute leptomeningitis is an infectious condition due to various organisms. The pneumococcus is the one found in the greatest number of cases, but many varieties have been described. In the epidemic meningitis the *Diplococcus intracellularis meningitidis* of Weichselbaum has been recognized as the cause. The infecting agent gains entrance either as a result of wounds, by way of the lymphatics, or by direct extension.

Serous leptomeningitis consists of round-cell infiltration of the membranes, with hyperemia and the exudation into the subarachnoid space and ventricles of a serous fluid. This may be slightly cloudy from leukocytes that are sometimes present. This form occurs in children in the course of infectious diseases, as scarlet fever and measles; and in adults after sunstroke. It is probably the beginning stage of an infectious inflammation in which the death of the patient has followed before further lesions have had time to develop.

Fibrinopurulent leptomeningitis is probably a later stage of the preceding. In the subarachnoid space there is a collection of pus and fibrin. This may increase until the sulci are marked out as yellowish bands, and eventually the surface of the brain may be covered by this purulent exudate. The process may be confined to local areas, or involve both hemispheres. If at the vertex, it is known as *cortical meningitis;* at the base, as *basilar meningitis.*

The pus may gain entrance into the ventricles, or it may

follow along the blood-vessels, particularly the middle meningeal, and involve the cortical substance with degenerative changes in both cells and fibers. Small hemorrhages may be present and discolor the exudate. The termination is usually fatal, but absorption and recovery may take place. There are, however, permanent structural changes, as a rule.

Epidemic cerebrospinal meningitis resembles the above form, except that it has a specific organism, the *Diplococcus intracellularis*, as its cause. It generally starts upon the convexity of the frontal lobes, and extends backward and downward, involving the basal membranes and those of the cord later on. Death may, however, take place so suddenly that distinct changes may not be noticeable.

The spinal changes may be more marked than those of the brain, the cord being covered by a thick yellowish layer of pus and fibrin. Occasionally the central canal may contain pus.

Chronic leptomeningitis is an inflammation of the pia, usually secondary to diseases of the brain or dura. There is a hyperplasia of connective tissue and round-cell infiltration. The thickening may be so great as to cause compression of the brain-substance or obliteration of venous channels. Large or small areas may be involved, and adhesions between the pia and the dura or the brain may form.

Tuberculous meningitis is more common in children than in adults, and is generally found upon the basilar surface. This location is so frequent that the term basilar meningitis refers to a tubercular process. This disease may be primary, but is, as a rule, secondary to tuberculosis elsewhere, particularly of the lung.

Upon the pia over the pons, about the optic chiasm, and along the Sylvian artery are found the miliary tubercles, the characteristic lesions of the process. They may also be noticed in the choroid plexus and the ependyma as a result of extension. The tubercles vary in color from gray to yellow, according to their age.

There is generally some exudate, either serofibrinous or purulent, especially if there has been a mixed infection by the pneumococcus. This may be so thick as to obscure the tubercles.

Most of the tubercles are found around blood-vessels, and consist at first of a cellular infiltration, with some thickening of the vessel-wall. Giant-cells are not as common as in tuberculosis elsewhere. As the disease persists, degeneration and caseation take place.

If the infection has been primary, there may be a single large tubercular area—a *tyroma*. Such a mass may be soft from liquefaction necrosis, or fairly firm; occasionally it may be the seat of calcareous infiltration.

Syphilis is found in the pia, usually in the form of gummata which may extend and involve the brain or the dura. This form is found as circumscribed, flattened thickenings that generally show necrotic processes.

Another form is characterized by a perivascular round-cell infiltration which may become diffuse. This portion of the pia may become quite thickened and grayish-red in color. Caseation takes place around the edge of the node, and the destroyed portion is gradually replaced by dense cicatricial tissue.

It may occur as a widespread leptomeningitis.

Tumors.—The Pacchionian bodies are numerous small, rounded, projecting structures found along the longitudinal sinus. They consist of fibrous tissue that originates within the arachnoid, but as they grow they force their way at times through the dura and cause a firm union of the membranes. There is also very frequently more or less atrophy of the skull, causing depressions into which these bodies fit. In places the bone may be greatly reduced in thickness. These bodies are found in nearly every adult body, and appear to be of no significance.

Endothelioma and *perithelioma* are found in the membranes, having originated from the cells of either the lymphatics or the blood-vessels. They may become sufficiently large to cause pressure symptoms, but are usually small. *Sarcoma* may occur in the form of angiosarcoma or cylindroma. *Fibroma*, *lipoma*, and *myxoma* are occasionally seen. *Cholesteatomata* are sometimes found in the pia, generally at the base of the brain. *Teratomata* are rarely encountered.

Secondary growths are not infrequent, either by direct extension or by metastasis.

Cysts are rare.

Parasites are unusual, but the echinococcus and the *Cysticercus cellulosæ* have been observed.

THE BRAIN

Malformations of the brain may be associated with deformities of the skull, or may occur independently. *Acrania* is an absence of the skull, but usually with preservation of the membranes and a small mass of nerve tissue. *Hemicrania* is an undeveloped condition of the skull and brain on one side. *Anencephaly* refers to a condition in which there is almost complete lack of brain-substance; it is usually associated with acrania. *Cephalocele* is a hernia of the brain-substance through fissues or openings.

Hypoplasia or *microcephaly* is a condition in which the brain is unusually small, but properly proportioned. It is frequently associated with some degree of external hydrocephalus. *Macrocephaly*, or increase in size of the brain, is generally due to a hyperplasia of the neurogliar tissue. *Porencephaly* refers to the presence of definite holes or depressions in the brain-substance. It may be the result of softening following infarction.

Hydrocephalus is a collection of fluid either within the ventricles of the brain or in the subarachnoid space. It may be *external* to the arachnoid, or *internal*, and may be *congenital* or *acquired*.

External hydrocephalus is frequently *ex vacuo* to supply by an exudate a loss of cerebral tissue.

Internal hydrocephalus is a collection of fluid within the third and lateral ventricles of the brain. The amount of fluid may vary greatly. The process generally begins before birth, and may cause serious obstruction to labor. The condition is generally bilateral. After birth, if the accumulation of fluid persists, there is a very typical deformity of the skull. The presence of the fluid within prevents the bones of the brain from uniting. The sutures are pushed

far apart, giving a peculiar bulging to the forehead. The head becomes quite large and round, the face small, and the eyes may project. The cerebral tissue, on account of the pressure, shows a marked flattening of the convolutions.

The dura and pia may be thin or thick, and the choroid plexuses of the ventricles may be hypertrophied or cystic.

The collection of fluid will or will not interfere with the mentality of the individual according to the amount that is present. In very marked cases it is incompatible with life, but, if less severe, the individual may live, although more or less of an imbecile.

The cause of this condition is not known, but by some it is thought to be due to alcoholism in the parents; to inflammatory conditions of ependyma and choroid plexus; to closure of the transverse fissure, causing obstruction to the escape of fluid from the ventricles; and to changes in the pressure within the cerebral veins.

FIG. 166.—CONGENITAL INTERNAL HYDROCEPHALUS, WITH MARKED ATROPHY OF THE WHITE SUBSTANCE (from Bollinger).

Acute acquired hydrocephalus is generally found as a result of basilar meningitis. The brain is pale, soft, and the convolutions flattened; the contained fluid is frequently gelatinous. The ependyma and choroid plexuses are injected, and if the process was tubercular, tubercles will be found. The substance of the brain will show under the microscope the presence of small areas of suppuration.

Chronic acquired hydrocephalus generally occurs late in the

course of epidemic meningitis or as a consequence of a chronic granular ependymitis.

Ependymitis may be either acute or chronic. The acute form is associated with acute meningitis, and in it there is a thickening and leukocytic infiltration of the ependyma and pia. In chronic ependymitis the surface is granular, the ependyma is thrown into folds and becomes much thicker on account of a hyperplasia of the contained neurogliar fibers.

Circulatory Disturbances.—*Anemia* of the brain is characterized by a pallor of the cortex and white substance as a result of the diminished amount of blood. It is due to general anemia, severe hemorrhage, disease of the blood-vessels, particularly atheroma, increased intercranial pressure, or to spasmodic contraction of the blood-vessels.

Acute Hyperemia.—The amount of blood in the brain is increased during its activity. Pathologically, it is found in beginning inflammations, in infectious diseases, acute delirium, sunstroke, etc. The blood-vessels in the pia are injected, the cortex is darker than normal, and minute hemorrhages may be present.

Passive hyperemia occurs in any of the conditions that prevent the blood escaping from the cerebral veins, as heart disease or local growths. The veins of the membranes are much distended, and the cortex and medulla are of a bluish tinge.

Edema of the brain is generally secondary to conditions causing passive congestion. There may be a slight edema that is soon taken up by the lymphatics. The fluid is most marked in the subarachnoid and ventricular spaces. The membranes are elevated, and the convolutions are flattened, The edematous fluid contains more albumin and is more cloudy than the normal. Indications of inflammation are usually present. This condition may be a terminal phenomenon. It is found in renal disease and in alcoholism. In the latter there is frequently a great excess of the fluid. Microscopically, there may be some proliferation of the endothelium, and around the blood-vessels there is some round-cell infiltration. Local edema is sometimes found in the

neighborhood of areas of softening. In acute hydrocephalus the internal capsules may be involved and transient hemiplegia follow.

Hemorrhage occurs in two forms, *minute* (*punctate*) or *massive*.

Punctate hemorrhages are small collections of blood formed by diapedesis of the erythrocytes or by rupture of a small vessel. They are generally found in the cortex, and occur in the course of inflammation of the brain, in various infectious diseases, and in toxic conditions, particularly lead-poisoning. They seldom cause any secondary disturbances.

Massive hemorrhages, unless traumatic, are commonly found to affect the branches of the middle cerebral artery. In these cases there has generally been a pre-existing disease of the vessel, the rupture usually taking place in a small aneurysm. It is commonly known as apoplexy. The internal capsule is almost always involved. The pons is quite frequently the seat of hemorrhage, and occasionally the cerebellum, but very rarely the medulla.

The size of the involved area depends upon the amount of blood extravasated and upon the density of the tissue. It is more diffused in the white than in the gray matter. The effects of the hemorrhage may be primary or secondary.

Primary effects are tearing and compression of the brain-substance. If the patient does not immediately die, softening occurs. As a result of the staining by the retained hemoglobin the area is known as red softening. Shortly after the blood escapes it undergoes coagulation, forming a cerebral hematoma. This acts as a foreign body and sets up an inflammatory reaction, with more or less hyperplasia of the surrounding neuroglia. The fluid portion finally becomes absorbed, the corpuscles broken down, and the pigment liberated, which stains the walls of the cavity. Occasionally a cyst filled with a clear fluid may form. If all fluids are absorbed, the walls of the cavity may come in contact and a scar result.

Other primary effects are distant ones in the form of paralysis, both motor and sensory, and generally on the side of

the body opposite to the seat of the hemorrhage. Although there may be a considerable return of the lost faculties, yet in a majority of cases permanent damage is done. This is due to the secondary effects—the *secondary degenerations.* These are systemic, and follow the direction of the nerve impulses. The commonest degeneration is one of the pyramidal tracts. The optic tract and fibers from the temporosphenoidal area may also be involved. In the brain there is finally loss of nerve-cells, without destruction of the neuroglia fibers.

As a result of traumatism, hemorrhages may take place in any part of the brain, with or without fracture of the skull. The hemorrhage may be found on the side of the head opposite to that where the blow was received.

Thrombosis and Embolism.—*Thrombosis* is most common as a result of embolism or of endarteritis. It may be found anywhere, but is probably more frequent in the basilar artery. From obstruction to the nutrition *encephalomalacia*, or softening of the brain, ensues.

Embolism commonly results from a breaking off of a part of a verrucosity or of a leaflet of one of the heart valves, especially the aortic. The greater number of the emboli pass along and finally lodge in the artery of the Sylvian fissure. If the embolus is so large as to remain at the beginning of the artery, there will be a large degenerated area. The corpus striatum, a large part of the internal capsule, and the anterior part of the optic thalamus will be involved. As different branches are obstructed, the areas of degeneration will vary. If the emboli are so small as to enter the posterior perforated space, the optic thalamus only will show small areas of degeneration.

Degenerations.—*Encephalomalacia*, or local softening of the brain, is found in ischemia, as a result of arteriosclerosis of the smaller vessels, in thrombosis and embolism, and in meningitis and encephalitis. The brain-substance breaks down and undergoes colliquation necrosis. The areas of softening are usually referred to by the color that they present. They are, however, not different processes, but merely different stages of the same condition.

White softening is a colliquation necrosis occurring when the blood-supply has been completely and permanently cut off. If this area is incised, the contents will escape, leaving an irregular cavity with ragged borders, and in it will be found some nerve-fibers and neuroglia. The escaped contents are composed of degenerated nerve-structures, with fat-droplets, granule-cells, and leukocytes.

Yellow softening may be due to an increased fatty degeneration occurring in white softening or a late stage of red softening.

Red softening is a breaking-down of nerve tissue accompanied by the extravasation of blood. It may be due to a hemorrhagic infarction or to diapedesis. The contents of the involved area are not generally as fluid as in the other forms of softening.

The areas of softening may vary greatly in size and in the time of their formation. The same process, however, goes on, the myelin sheaths degenerate, the axis-cylinders may disappear, compound granule-cells appear, and finally the neurogliar fibers may soften. The broken-down tissue may be slowly absorbed, leaving a cyst with smooth, well-defined walls, and clear contents. The cysts may become encapsulated, or through absorption scar tissue form.

Encephalitis, or inflammation of the brain-substance, is peculiar on account of the tissue that is involved. It differs from inflammation elsewhere in that conditions of degeneration or softening are associated.

Encephalitis may be acute or chronic, diffuse or circumscribed. The causes of the condition are many. It may result from *injury without infection;* in this form there is a hemorrhagic extravasation, followed rapidly by necrosis. Around the necrotic tissue is a hyperemic zone in which there is some transmigration of leukocytes, and slight proliferation of the connective tissue of the sheaths surrounding the vessels. *Injury with infection* generally affects the membranes primarily, but soon involves the brain-substance. There is a marked leukocytic infiltration along the blood-vessels, and the brain-substance undergoes degenerative processes. In-

flammation of the brain may also be secondary to infectious disease elsewhere in the body. In *hematogenic focal encephalitis* specific micro-organisms are brought to the brain by the blood. Numerous areas are found in which the blood-vessels are distended and interstitial hemorrhages are present. The lymphatics contain many leukocytes, and the nerve-tissues rapidly degenerate. If the patient survives long enough, *suppurative encephalitis* may ensue. This form is generally due to infection by the pneumococcus, streptococcus, or staphylococcus, and true abscesses, either single or multiple, are formed. If the extension has been by the blood, they will be multiple; if by direct continuity, as from middle-ear disease, they will be single. The size may vary greatly—they are generally about as large as a walnut. They are most frequent in the cerebrum, but may be found in the cerebellum and rarely in the pons and medulla. When the acute processes subside, a proliferation of the surrounding neuroglíar tissue may occur and encapsulate the abscess. *Toxic encephalitis* is caused by the presence, in the circulating blood, of certain substances that act upon the nerve-cells and cause various changes that can be recognized by the employment of special methods of study. These changes are found in the cells of both the brain and spinal cord in diphtheria, tetanus, lead-poisoning, and hydrophobia, also to some extent in alcoholism. *Chronic encephalitis* or *sclerosis* occurs in all cases of injury to the brain in which recovery occurs. There is a chronic hyperplasia of the neuroglia, which may be local or diffuse. In *multiple localized sclerosis* there are numerous scattered foci of degeneration, associated with hyperplasia of the neuroglia. They are sharply defined, slightly dense to the touch, and grayish or pinkish in color. *Diffuse sclerosis* is characterized by widespread areas of neurogliar hyperplasia. It is more common in children, and does not seem to be due to toxic or inflammatory conditions. It may be sharply circumscribed and resemble glioma. At first the brain may appear hypertrophied, but later, as atrophy of the nerves occurs, it becomes smaller. Certain lobes or convolutions may be involved,

and there is always considerable degeneration of the nervous structures.

Tuberculosis of the brain may be primary or be secondary to tuberculosis of the meninges. When secondary, there are generally many small tubercles along the perivascular tissues, particularly along the small vessels of the anterior and posterior perforated spaces. Primary tuberculosis is hematogenic, and occurs as single lesions. It is more common in children. The tubercle gradually becomes larger, and caseous degeneration occurs, is rather dense, yellowish in color, and dry, and sometimes undergoes calcification or again contains a yellowish purulent-like matter. The growth increases in size by the formation and aggregation of new tubercles at the periphery of the original focus. These large areas are called *tyromata.*

Syphilis of the brain generally appears as a gumma that has originated within the pia and extended to the brain. The gumma is at first grayish or reddish-gray, but very soon undergoes a secondary necrosis and caseation. Recovery takes place with the formation of a dense cicatrix. Syphilitic endarteritis is sometimes found and gives rise to secondary degenerations with softening.

Tumors of the Brain.—The most frequent form of those found is the *glioma.* It is commonly found in the cerebrum, the cerebellum, the pons, and medulla. It is thought to never originate from the pia. The glioma appears as a diffuse, poorly defined area, pinkish or reddish in color from the numerous blood-vessels that are present. The tumor may be composed purely of neurogliar tissue, without any nerve-cells or fibers present. Occasionally ganglionic cells, isolated or in groups, are found embedded in the neoplasm; such tumors are known as *gangliomata* or *neurogliomata.* Microscopically gliomata are made up of cells from which numerous filaments project and which compose the groundworks of the tumor.

Some gliomata are considered as sarcoma, but as the tumors arise from different embryonal layers, such a combination could hardly occur. The sarcoma differs clinically

from the ordinary glioma in being of a more rapid growth and giving metastases.

Sarcoma is fairly frequent, and commonly arises from the pia or from the connective tissue around the blood-vessels. It is generally rather circumscribed, and may be encapsulated. The commonest variety is the small round-cell, but spindle-cell and giant-cell forms occur. *Angiosarcoma* is not infrequent, and the *perithelioma* or *myxangiosarcoma tubulare* is fairly common. *Psammosarcoma,* in which infiltration of lime-salts takes place, is occasionally encountered. It is generally small and gritty. *Endothelioma* is found in the pia and sometimes in the choroid plexuses.

Other forms of primary tumors are rare. As secondary growths, sarcoma and carcinoma are fairly frequent.

Parasites are rare; the echinococcus and the *cysticercus cellulosæ* have been found.

THE PITUITARY BODY

Hypertrophy is uncommon, but it occurs in cretinism, myxedema, and acromegaly. If the thyroid gland is removed it is thought that the pituitary body sometimes enlarges. The acini may contain a large amount of colloid material.

Hyperemia may occur, and in cases of passive congestion there may be considerable edema. *Hemorrhage* may take place just before death, and erythrocytes will be found in the connective tissue.

Inflammation is rarely primary, is usually secondary, as a result of extension, and suppuration may occur. The dura covering the gland may become much thickened, and as a result the pituitary body atrophies or undergoes a fibrous change.

Tuberculosis in the form of miliary foci and *syphilis* in the form of gummata have been observed.

Tumors.—*Sarcomata,* round-cell or spindle-cell, are sometimes found. They develop apparently from the capsule of the gland and destroy the substance. They seldom infiltrate the surrounding tissue and do not give metastases.

Adenoma causes a general enlargement and is the growth

most commonly found associated with akromegaly. It consists of long, tortuous tubes, and causes atrophy of the posterior or nervous lobe.

Teratoid growths have been described.

Cysts are generally the result of retention of the colloid material. The epithelial cells disappear and the follicles distend. The cysts may grow to the size of a hen's egg.

CHAPTER XXVII

DISEASES OF THE SPINAL CORD

Circulatory Disturbances.—*Anemia* of the cord may be due to pressure from neoplasms or to obstruction of small blood-vessels by disease or thrombosis. Embolism is followed by necrosis. In pernicious anemia degenerative changes in the posterior columns of the cord may occur.

Hyperemia is present in all inflammations of the meninges or cord. *Passive hyperemia* is present in chronic heart and lung disease. Antemortem congestion is difficult to differentiate, as there is nearly always hypostasis of the blood into the spinal vessels.

Hemorrhage into the cord is less common than in the brain. It may be punctate or massive. The punctate form occurs in death from convulsions, as in tetanus, after injuries, in degenerated areas, about tumors, after extreme congestion, and in other conditions. Massive hemorrhages are seldom larger than a small marble. They may find a way along the longitudinal fibers or occasionally rupture into the central canal.

The changes that take place if the individual lives are similar to those occurring in the brain under like conditions.

Myelitis, although strictly signifying an inflammation of the spinal substance, is used to indicate any form of degeneration present in the cord. It may be primary or secondary. The *primary* form occurs at the seat of the injury, and is frequently a circumscribed condition. *Secondary* degeneration depends upon primary changes elsewhere, and is due to the destruction of nerve-cells or axis-cylinders. It is generally considerably more extensive than a primary degeneration. The degenerated areas may be white, red, or yellow, accord-

ing to the amount of blood present and the stage of the softening. In the early stages the involved tissue is swollen and pinkish, and minute hemorrhages may be present. The tissue is at first softened, but finally becomes firmer as fibrous changes occur. Microscopically the myelin is found to be destroyed, breaking down into droplets that stain with osmic acid. The axis-cylinders swell up and degenerate, the nerve-cells show enlargement and finally disappearance of their nuclei. The tissues generally become disorganized and give rise to *white softening*, there being no change in color. If the damage to the cord has been such as to cause extravasation of blood into the involved area, it will be known as *red softening.* As the blood is destroyed the pigment is set free, with the formation of areas of *yellow softening.*

In *purulent myelitis* there will be found a round-cell infiltration in the perivascular spaces, pus in the pia mater, and degeneration of the neighboring nerve-tissues. The ganglion-cells, though very resistant, sooner or later show degenerations.

When the acute processes subside, there is some absorption of the broken-down tissues and a hyperplasia of the neuroglia and connective tissue, constituting the early stage of *sclerosis.* The newly formed tissue is grayish in color, firm, dense, and dry. There is probably little, if any, attempt toward the regeneration of the nerve-fibers.

Myelitis may be traumatic, infectious, toxic, or nutritional.

Traumatic myelitis may result rapidly, but it is usually slow, as a result of compression of the cord by tumors or collections of fluid in the spinal canal. The degeneration generally extends entirely across the cord, being known as *transverse myelitis.* There are usually three stages, that of red softening, of yellow softening, and of gray degeneration, and connective-tissue hyperplasia.

Infectious myelitis may be transverse or disseminated, particularly the latter. Micro-organisms are generally present in the lesions.

Varieties of Myelitis.—When the spinal membranes are inflamed, the condition is known as *spinal meningitis;* if the membranes and cord are both affected, *meningomyelitis.* Inflammation of the cord alone is known as *myelitis;* disease of the white substance is *leukomyelitis;* if the gray matter, *poliòmyelitis.*

Myelitis is referred to as *central* when arising from disease of the central canal; *diffuse* if it involves the entire cord; *transverse* when a small section is entirely affected; *disseminated* when there are numerous small areas more or less widely separated.

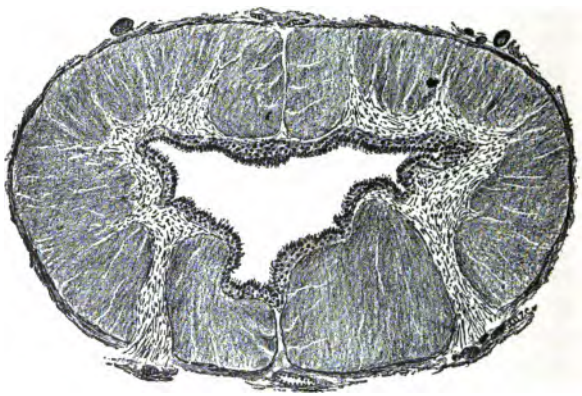

FIG. 167.—HYDROMYELIA (PARTLY DIAGRAMMATIC) (Stengel).

It may be *simple*, *hemorrhagic*, or *purulent*, or, according to development, *acute* or *chronic.*

Hydromyelia is a condition in which the central canal of the spinal cord is dilated by an increased amount of cerebrospinal fluid. The dilatation may be irregular, usually being more marked in the lumbar cord. The canal may be round, slit-like, or triangular, and is commonly lined by ependymal cells, a condition that does not exist normally. Sometimes the canal may be double or even triple, this being more frequent in the lumbar region. *Hematomyelia* refers to the

presence of blood in the central canal; *pyomyelia*, when pus is present.

Syringomyelia is characterized by a central dilatation of the spinal canal resulting from the proliferation of the glia about the central canal and subsequent degeneration of the newly found tissue.

The appearance is somewhat similar to that in hydromyelia, but the canal is not lined by ependymal cells.

The etiology of the condition is unknown. There is an extensive proliferation of gliar tissue around the central canal, probably beginning in the cervical portion, but extending down the cord. This tissue rapidly degenerates and liquefies. The cavity is generally posterior to the center of the cord, and may be so large as to leave merely a thin layer of nerve tissue surrounding it. The canal in the early stages is filled with a brownish, gelatinous mass, which eventually undergoes liquefaction, leaving the canal filled with clear fluid.

The extent of the secondary degeneration in the spinal cord and in the anterior and posterior nerve-roots will depend upon the size of the lesion and the amount of pressure exerted. Entire columns of the cord and anterior and posterior nerve-roots may be destroyed in severe cases.

Tuberculosis of the cord commonly involves the meninges, and secondarily extends into the nervous tissues; it is a *meningomyelitis*. Tubercles are present in varying numbers, and soon cause thickenings and necrosis. Disseminated tubercles may be seen in both the white and the gray matter, but are usually microscopic. Primary tuberculosis may occur in the form of a single circumscribed caseous mass.

Syphilis of the cord usually appears as a thickening of the membranes, especially of the dura. Involvement of the pia and arachnoid is uncommon. There is found a marked endarteritis, and the formation of thrombi is quite frequent. Areas of cheesy degeneration are due to the breaking-down of the diseased tissue.

Tumors of the Cord.—The most common form is the *glioma*, as occurring in syringomyelia. It infiltrates the

nerve tissue along the posterior portion of the cord. It seldom occurs as a circumscribed growth. *Sarcoma, cylindroma*, and *fibroma* are very rare, but have been observed.

Tumors of the spinal meninges are more common. Practically all varieties have been found.

Cysts are extremely rare, but both the echinococcus and the cysticercus have been reported.

Spinal Meningitis.—*Pachymeningitis*, or acute inflammation of the spinal dura mater, is commonly due to neighboring inflammations or to traumatism. In *external pachymeningitis* there is an exudate, cellular or fibrinous, upon the external surface. Abscesses may form and destroy by pressure the neighboring cord. *Internal pachymeningitis* is generally secondary to tubercular or syphilitic disease of the pia and the bones. There is a marked fibrous exudate, with adhesions between the dura and the underlying membranes. *Hemorrhagic pachymeningitis* is internal, and is similar to the process occurring in the brain. It is characterized by a reddish layer of granulations in which many of the capillaries have ruptured.

Chronic hypertrophic cervical pachymeningitis is a localized thickening of the dura mater in the cervical region. The pia and the arachnoid are also involved. Compression of the cord and secondary degenerations may ensue.

Leptomeningitis, or acute inflammation of the spinal pia and arachnoid, is generally secondary to cerebral meningitis, especially in the epidemic cerebrospinal form. It may be due to local injury or diseases of the bone. There is an exudation, serous, fibrinous, or purulent, upon the inner surface of the dura and the subarachnoid space. The inflammation may be local or involve the greater length of the cord. The tissue of the cord is commonly affected, and extensive round-cell infiltration occurs in the anterior commissure and in the perivascular connective tissue.

SPECIAL DISEASES OF THE SPINAL CORD

Disseminated or **multiple sclerosis** occurs in both the brain and the spinal cord, and is characterized in the early

stage by the presence of many softened areas. These vary in size, are grayish in color, are more frequently found in the white matter than in the gray. There is a degeneration of the myelin and of the cells, but the axis-cylinders remain uninvolved for a long time. Hyaline degeneration of the blood-vessels is commonly present. As the disease progresses, the softened areas are gradually replaced by a hyperplasia of the glia tissue. There is also atrophy of the nerve-cells and of some of the axis-cylinders.

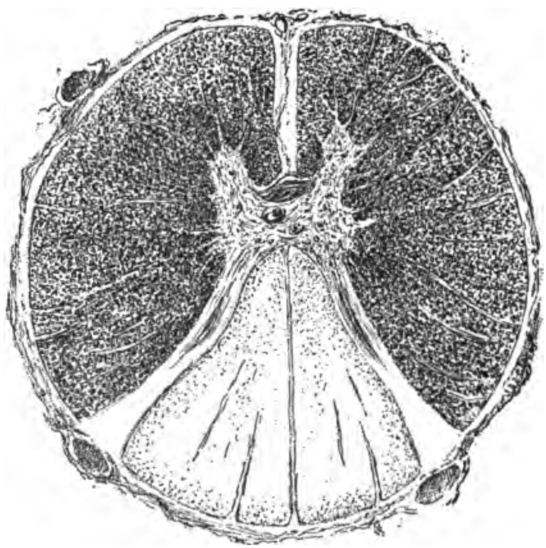

FIG. 168.—TABES DORSALIS (Collins).

The etiology of this disease is obscure. It is found in syphilis, in acute infectious diseases, in chronic metallic poisoning, and in injuries.

Posterior sclerosis, tabes dorsalis, or **locomotor ataxia,** is a condition of sclerotic changes in the posterior columns. The present opinion is that it is the result of primary disease of the posterior nerve-roots. This is thought by many to

depend generally upon syphilitic infection, but it occurs in traumatism and possibly in some of the infectious fevers. The lumbar portion is more commonly affected than the dorsal, and lastly the cervical. The degeneration usually develops in the lumbar cord, in the posterior nerve-roots. In the dorsal region there are also two areas of degeneration in the column of Burdach and in the cervical region; the chief involvement is in the columns of Goll.

There is atrophy of the nervous tissue, with increase of the neuroglia. The myelin sheaths break down and expose the axis-cylinders, which resist the degenerative processes longer than the other tissues.

The lesions may not only affect the cord and peripheral nerves, but also involve areas in the brain and in the optic, oculomotor, and trigeminal nerves.

There are also degenerations nearly always present of the sensory nerve-endings.

The main symptoms are girdle pains, loss of knee-jerk, Argyll-Robertson pupils, loss of sensation and tactile sense.

Friedreich's disease, or **hereditary ataxia,** is a variety of posterior sclerosis that usually begins about the seventh year, and involves several members of a family. There is a hypoplasia of the cord or the cerebellum, and sclerosis of the posterior columns of the cord. The fibers in the column of Goll and the greater part of those in the column of Burdach degenerate, and the cells in the column of Clark are involved at times. There is also some degeneration of the direct cerebellar tract and of the lateral pyramidal columns as well. The lesions are most marked in the lower part of the cord.

Acute anterior poliomyelitis is characterized by degeneration and sclerosis of the anterior horns of the gray matter of the spinal cord. It occurs chiefly in children about three years old, but at times affects adults.

The cause is unknown, but the processs is that of an acute inflammation. It is apparently either infectious or toxic in its origin and is distributed by the blood-vessels. The disease usually begins rapidly, and is accompanied by chills and fever.

The lesions may be unilateral or bilateral, and are more common in the lumbar region. Early in the disease the blood-vessels of the anterior horns of the gray matter are distended, and the perivascular lymph-spaces filled with round-cells. Small interstitial hemorrhages may be present in the anterior horns. The ganglion-cells become larger, granular, and cloudy, often vacuolated, and altered in their staining reactions. The cells eventually become completely degenerated and disappear, the medullated nerves lose their covering, and many are destroyed. Neurogliar hyperplasia

FIG. 169.—CHRONIC ANTERIOR POLIOMYELITIS (Collins).

occurs in the involved areas, and the gray matter may become much indurated.

Chronic anterior poliomyelitis or **progressive muscular atrophy** occurs generally in adults, and is characterized by atrophy and disappearance of the motor cells of the anterior horns of the spinal cord. The small muscles of the hand are the first to undergo atrophy, then those of the arms, shoulders, and body.

The diaphragm may become involved and death result. The change is one of fatty degeneration.

The lesions generally appear in the cervical and upper dorsal portions of the cord, and extend along the anterior cornua in both directions. When the medulla is affected, the resulting condition is known as *bulbar palsy.*

Bulbar palsy is similar to the above except that it occurs in the medulla instead of in the cord, and affects the ganglia of the hypoglossus, glossopharyangeal, spinal accessory. vagus, facial, abducens, and motor portion of the trigeminus,

Amyotrophic lateral sclerosis is a disease in which

FIG. 170.—COMBINED POSTERIOR AND LATERAL SCLEROSIS (Collins).

there is a degeneration of the peripheral motor nerves as well as an atrophy of the motor cells in the anterior horns of the gray matter of the cord. There is also more or less degeneration of the pyramidal columns. The muscles undergo the same changes as in progressive muscular atrophy.

The degenerations begin in the sacral and lumbar portions of the cord and extend upward.

Secondary Degenerations of the Spinal Cord.—The microscopic changes are those that have already been de-

scribed. The degenerations result from lesions in the brain or cord, and when in the cord are described as either ascending or descending, according to the tracts affected.

Descending degeneration is the usual result of disease of the cerebral cortex and internal capsule. It involves the motor tracts and the anterior and lateral pyramidal columns. If the lesion is unilateral and above the decussation, the anterior tract on the same side and the lateral pyramidal tract on the opposite side will be affected.

Ascending degeneration usually follows transverse myelitis and involves the sensory tract, the posterior columns below, and the columns of Goll above.

THE PERIPHERAL NERVES

Atrophy may result from pressure, from inflammation, or from an interruption in the continuity of the nerve. The myelin sheaths undergo degeneration, and later on the axis-cylinders break down.

Degeneration of the nerves is with difficulty separated from inflammation. When non-inflammatory, is a *simple* degeneration; otherwise an *inflammatory* degeneration. The inflammatory ones are known as *parenchymatous* neuritis, in contradistinction to the *interstitial*, which involve the nerve-sheaths.

Degeneration is found in injuries, in infectious diseases, and in intoxications. Certain nerves or sets of nerves may be involved in the different conditions, as those of the pharynx in diphtheria, those supplying the extensor muscles of the forearm in lead-poisoning, or the cord in syphilis.

The degenerative changes may appear within twenty-four hours after an injury. The myelin sheaths become granular and cloudy, and finally break down into droplets. Larger drops form, fatty degeneration occurs, and leukocytes make their appearance. The axis-cylinders resist for a longer time, but they become nodular, vacuolated, and break up. The degeneration occurs more rapidly in the distal than in the proximal end. Regeneration may take place, but the nerve is usually replaced by a cord of fibrous tissue.

Neuritis.—The so-called *parenchymatous* neuritis is a degeneration of the nerve-fibers without involvement of the connective tissue. *Interstitial* neuritis is a true inflammatory process affecting the connective tissue.

Acute interstitial neuritis is due to the same causes as bring about the degenerations. It is characterized by an exudation into the endoneurium and perineurium. There are edema and congestion, with an infiltration of round-cells and at times pus-cells. At the same time there is commonly degeneration of the nerve-fibers. The nerves are swollen and reddened.

Chronic neuritis is interstitial and follows an acute attack, or is due to various infections and intoxications, as chronic lead- or alcohol-poisoning. There is a marked hyperplasia of the connective tissue, with associated degeneration and atrophy of the nerve-fibers.

Tuberculosis of the nerves is due to secondary involvement through extension. The roots of the nerves are generally affected. There are a hyperplasia of the connective tissue and a secondary degeneration of the nerve-fibers.

Syphilis of the nerves occurs commonly in the nerve-roots. It is characterized by a round-cell infiltration at first, and later by a marked hyperplasia of connective tissue, associated with atrophy and degeneration. Gummata have been observed in the cranial nerves.

Leprosy of the nerves is characterized by nodular lesions along their course. There is a proliferation of the bacilli, with the formation of nodes in the fibers, accompanied by cellular infiltration with connective-tissue hyperplasia and degenerations. The lepra bacilli can be found within the tissues.

Tumors.—*Neuromata* are the most frequent form of them, the *false neuroma*, which is more common than the true, is a growth taking place within the connective tissue of the nerve; it is similar to a fibroma.

Sarcomata occur, but are rare.

The malignant tumors may occur as secondary growths.

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